DB Name	Query	Hit Count	Set Name
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	((pharmaceutical composition) or kit) and (Rituxan or rituximab)	15	L15
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	L13 and ((B cell) adj lymphoma)	96	L14
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	((pharmaceutical composition) or kit) and (CD20 or Rituxan or rituximab)	377	L13
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	L10 and (graft or transplantation)	72	L12
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	(immunosuppression) same (CD20 or Bp35)	0	L11
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	(immunosuppression) and (CD20 or Bp35)	93	L10
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	L7 and (graft or transplantation)	60	L9
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	L7 and ((blocking or suppress) adj (immune response))	2	L8
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	L6 and (immune response)	97	L7
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	L5 and (antibody or Rituxan or rituximab)	128	L6
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	L4 and (antagonist)	131	L5
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	(CD20 or Bp35)	597	L4
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	Stewart-timothy-A$.in.	13	L3
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	Kunkel-lori-a$.in.	0	L2
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	Grillo-Lopez-antonio-J$.in.	0	L1

```
    23dec02 11:35:19    r259876 Session D447.1
         $0.35    0.100 DialUnits File1
$0.35  Estimated cost File1
$0.05  TELNET
$0.40  Estimated cost this search
$0.40  Estimated total session cost   0.100 DialUnits


SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2002/Nov W3
*File 155: For updating information please see Help News155. Alert
feature enhanced with customized scheduling. See HELP ALERT.
  File 159:Cancerlit  1975-2002/Oct
         (c) format only 2002 Dialog Corporation
  File   5:Biosis Previews(R)  1969-2002/Dec W3
         (c) 2002 BIOSIS
*File   5: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File  73:EMBASE  1974-2002/Dec W3
         (c) 2002 Elsevier Science B.V.
*File  73: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.

      Set  Items  Description
      ---  -----  -----------
?s (anti-CD20 or anti-Bp35 or Rituximab) (s) (graft or transplant or translantation)
             15  ANTI-CD20
              0  ANTI-BP35
           3090  RITUXIMAB
         374795  GRAFT
         164500  TRANSPLANT
             15  TRANSLANTATION
      S1    266  (ANTI-CD20 OR ANTI-BP35 OR RITUXIMAB) (S) (GRAFT OR
                 TRANSPLANT OR TRANSLANTATION)
?s s1 and (treatment or therapy)
            266  S1
        4348605  TREATMENT
        4967834  THERAPY
      S2    253  S1 AND (TREATMENT OR THERAPY)
?rd
...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...examined 50 records  (200)
...examined 50 records  (250)
...completed examining records
      S3    133  RD (unique items)
?s s3 and review
            133  S3
        1365660  REVIEW
      S4      6  S3 AND REVIEW
?t s4/3,k/all

 4/3,K/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11060398   21064168   PMID: 11122838
  Biotherapy for lymphoma.
  McLaughlin P
  Department of Lymphoma/Myeloma, University of Texas MD Anderson Cancer
Center, 1515 Holcombe Boulevard, Box 68, Houston, TX 77030, USA.
pmclaugh@notes.mdacc.tmc.edu
  Current oncology reports (United States)  Mar 2000, 2 (2) p157-62,
ISSN 1523-3790  Journal Code: 100888967
  Contract/Grant No.: CA16672; CA; NCI
  Document type: Journal Article; Review; Review, Tutorial
```

contamination by lymph[redacted] cells. Molecular remission, [redacted]as measured by bone-marrow bcl-2 clearance, has been achieved in 7/7 patients with follicular NHL at 1 year after *treatment* with ASCT using *rituximab* as an 'in vivopurse', followed by *rituximab* maintenance. Early clinical outcomes are also encouraging.

4/3,K/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12904440 21828528 PMID: 11840155
***Rituximab*: enhancing stem cell *transplantation* in mantle cell lymphoma.**
Gianni A M; Cortelazzo S; Magni M; Martelli M
Instituto Nazionale Tumori, Milan, Italy.
Bone marrow transplantation (England) Feb 2002, 29 Suppl 1 pS10-3, ISSN 0268-3369 Journal Code: 8702459
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

***Rituximab*: enhancing stem cell *transplantation* in mantle cell lymphoma.**
... poorly to standard chemotherapy regimens used in non-Hodgkin's lymphoma. As a result, a combination of high-dose chemotherapy (HDT) with autologous stem cell *transplantation* (ASCT) is being investigated in patients with MCL. So far, however, there is no evidence for long-term remission -- believed, in part, to be due...

...cells. Many ex-vivo purging methods have been developed to remove tumour cells, but these are complicated, time-consuming and expensive. This study describes an *in* *vivo* *purging* method using *rituximab* to produce a tumour-free stem cell product for re-infusion following HDT. The regimen is split into a purging phase and a myeloablative phase, which together consist of four-step high-dose sequential chemotherapy (sHDT) and six infusions of *rituximab* immunotherapy. The sHDT comprises cyclophosphamide, cytosine arabinoside, melphalan and mitoxantrone plus melphalan. There are two separate stem cell harvests and three reinfusions. In a pilot study 28 patients with untreated MCL received standard chemotherapy followed by sHDT with *rituximab* *in* *vivo* *purging*. Preliminary results indicate that in PCR analyses of leukaphereses from 20 assessable patients, 100% lymphoma-negative harvests were achieved following *in* *vivo* *purging*. PCR analyses of the bone marrow following the four-step high-dose regimen with purging and *transplantation* showed that all patients achieved molecular remission. After a median follow-up of 22 months (range 10--42 months), two patients had died while 26 were alive and disease free. This method allows efficient *in* *vivo* *purging* in the context of an effective chemotherapy regimen and may have a role as first-line *therapy* in MCL patients who respond poorly to standard *treatment*.

4/3,K/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12904439 21828526 PMID: 11840153
Autologous stem cell transplantation in follicular non-Hodgkin's lymphoma.
Pettengell R
Department of Haematology, St George's Hospital Medical School, London, UK.
Bone marrow transplantation (England) Feb 2002, 29 Suppl 1 pS1-4, ISSN 0268-3369 Journal Code: 8702459
Document type: Journal Article
Languages: ENGLISH

Main Citation Owner: NL
Record type: In Process

The failure of conventional chemotherapy to improve overall survival rates in follicular non-Hodgkin's lymphoma (NHL) has led to the development of alternative *treatment* regimens. One such regimen is high-dose chemotherapy (HDT) with autologous stem cell *transplantation* (ASCT). In ASCT stem cells, harvested predominantly from peripheral blood, are used to repopulate the haemopoietic system after high-dose chemotherapy. Comparison of failure-free...
... the effect on relapse is unclear. Allogenic stem cell transplants have been associated with a reduced risk of relapse, but this is offset by increased *transplant* -related mortality. The most promising strategy to reduce the rate of relapse following ASCT is *in* *vivo* *purging* using *rituximab*, a monoclonal antibody to CD20. *Rituximab* mobilises mechanisms to kill lymphoma cells, and causes a rapid depletion of B cells from peripheral blood. *Rituximab* has demonstrated good efficacy as monotherapy in patients with both aggressive and indolent lymphoma and has shown very high response rates (>95%) when used in...

4/3,K/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11017622 21011535 PMID: 11128813

Immunotherapy with *rituximab* during peripheral blood stem cell *transplantation* for non-Hodgkin's lymphoma.

Flinn I W; O'Donnell P V; Goodrich A; Vogelsang G; Abrams R; Noga S; Marcellus D; Borowitz M; Jones R; Ambinder R F
Johns Hopkins University, Baltimore, Maryland, USA. iflinn@jhmi.edu
Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation (United States) 2000, 6 (6) p628-32, ISSN 1083-8791 Journal Code: 9600628
Document type: Clinical Trial; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Immunotherapy with *rituximab* during peripheral blood stem cell *transplantation* for non-Hodgkin's lymphoma.

... neoplastic cells. Administration of a lymphoma-specific monoclonal antibody before collecting stem cells may be one way of reducing the contamination. Similarly, an antibody after *transplantation* at a time of minimal residual disease may increase the efficacy of the procedure. The objective of this study was to determine the safety of using *rituximab* as both an *in* *vivo* *purging* agent and a posttransplantation adjuvant. Eligible patients with lymphoma received 375 mg/m2 *rituximab* intravenously IV) on day 1, 2.5 g/m2 cyclophosphamide IV on day 4, and 10 microg/kg per day filgrastim starting on day 5 and continuing until completion of leukapheresis. Patients subsequently received a standard preparative regimen and then received 375 mg/m2 *rituximab* IV 7 days after platelet independence was achieved. Twenty-five patients (14 men, 11 women; median age, 51 years) were enrolled. Of the 25 patients...

... with a sensitive polymerase chain reaction assay, 6 of 7 stem cell products tested were free of tumor contamination. All patients engrafted promptly, and the *rituximab* infusions were well tolerated. Transient neutropenia of uncertain etiology occurred in 6 patients a median of 99.5 days post-*transplantation* . An additional patient developed progressive pancytopenia. *Rituximab* used as an *in* *vivo* *purging* agent and adjuvant immunotherapy with peripheral blood stem cell *transplantation* for non-Hodgkin's lymphoma is a well-tolerated regimen. However, the ultimate determination of efficacy will require the results of ongoing studies.
Descriptors: Antibodies, Monoclonal--administration and dosage--AD; *Antineoplastic Agents--administration and dosage--AD; *Hematopoietic Stem

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The unconjugated anti-CD20 monoclonal antibody, *rituximab*, has quickly become an accepted *treatment* approach for a variety of B-cell malignancies. New directions for *rituximab* include its use in innovative doses and schedules, and in combination with either cytokines or chemotherapy. Other unconjugated antibodies (eg, CAMPATH-1H and anti-CD22) are available or in development. Radioimmunotherapy is another rapidly evolving field. In addition to *therapy* with monoclonal antibodies, other biotherapy approaches are being explored. The most widely utilized cytokine is still interferon-alpha. In general, other cytokines (eg, interleukin-2 ...

... immunotherapeutic approach. Exciting research is ongoing that exploits the host T-cell response, especially the development of vaccine strategies, and innovations in allogeneic stem cell *transplant* . The role of antigen-presenting cells (viz, dendritic cells) is also discussed in this *review* . A broad ability to exploit the immune system will hopefully soon be in our grasp.

Descriptors: Antibodies, Monoclonal--administration and dosage--AD; *Antineoplastic Combined Chemotherapy Protocols--administration and dosage --AD; *Immunotherapy--methods--MT; *Lymphoma, B-Cell--*therapy*--TH; Combined Modality *Therapy*; Cyclophosphamide; Doxorubicin; Lymphoma, B-Cell--mortality--MO; Prednisolone; Prognosis; Randomized Controlled Trials; Survival Analysis; *Treatment* Outcome; Vincristine

4/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10992265 20574430 PMID: 11125287

[Immunotargeting of tumors: state of the art and prospects in 2000]

Immunociblage des tumeurs: situation et perspectives en 2000.

Pelegrin A; Xavier F; Barbet J; Bartholeyns J; Baty D; Buchegger F; Chatal J F; Dufief F; Gurreau D; Gruaz-Guyon A; Lamotte D; Leserman L; Mach J P; Robert B; Saccavini J C; Teillaud J L; Teulon I

JE2167 Universite Montpellier I, Immunociblage des Tumeurs et ingenierie des anticorps, centre de recherche en cancerologie, 34298 Montpellier Cedex 5, France.

Bulletin du cancer (FRANCE) Nov 2000, 87 (11) p777-91, ISSN 0007-4551 Journal Code: 0072416

Document type: Journal Article; Review; Review, Academic ; English Abstract

Languages: FRENCH
Main Citation Owner: NLM
Record type: Completed

...antigens shows now important clinical developments. This is mainly due to encouraging therapeutic results which have obtained using humanized antibodies such as the anti-CD20 *rituximab* in follicular B lymphomas and the anti-DrbB2 herceptin in breast carcinomas. Thanks to genetic engineering it is possible to *graft* variable or hypervariable regions from murine antibodies to human IgG, and even to obtain fully human antibodies by using either transgenic mice containing a large...

... of antibodies played a major role to demonstrate the tumor immunotargeting specificity and remains attractive for the diagnosis by immunoscintigraphy as well as for the *treatment* by radioimmunotherapy of some cancers. In this *review*, the current results and the prospects of diagnostic and therapeutic uses of anti-tumor antibodies and their fragments will be described. Concerning diagnosis, 123-iodine...

... Immuno-PET (positron emission tomography) could enhance the sensitivity of this imaging method. Radio-immunoguided surgery and immunophotodetection

are attractive techniq still under evaluation. Con ning *therapy*, 131-iodine labeled anti-CD20 antibodies gave spectacular results in non-Hodgkin's B lymphomas. In solid tumors which as less radiosensitive, radioimmunotherapy could concern...

4/3,K/3 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13580992 BIOSIS NO.: 200200209813
Rituximab in lymphoma: A *review* of a province-wide initiative after one year.
AUTHOR: Cheung Matthew C; Meyer Ralph; Hux Jan; Evans William(a); Nefsky Marilyn(a); Imrie Kevin R(a)
AUTHOR ADDRESS: (a)Cancer Care Ontario, Toronto, ON**Canada
JOURNAL: Blood 98 (11 Part 1):p432a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

Rituximab in lymphoma: A *review* of a province-wide initiative after one year.

...ABSTRACT: centres and smaller communities. New cancer therapies are funded centrally by a state agency, Cancer Care Ontario (CCO), to ensure universal access throughout the province. *Rituximab* has been funded for use as monotherapy in indolent lymphomas since April 2000. We conducted a retrospective *review* of *rituximab* use over the first year of drug availability to assess the nature and outcome of *treatment* in Ontario. Criteria for approval of funding were: patients with follicular, mantle cell, or other CD20-positive indolent B-cell lymphomas who progressed after anthracycline or purine analogue chemotherapy, or who were unable to tolerate further chemotherapy. Funding for retreatment with *rituximab* was available for responding patients provided retreatment was not required within 1 year of initial *therapy*. The CCO database captures all non-clinical trial use of *rituximab* in Ontario that meets these eligibility criteria. Between April 1, 2000 and March 31, 2001, 230 patients were treated with *rituximab*. The mean patient age was 60.7 (range 22 to 83 years); 58.8% were male. The majority of patients were treated outside of a...

...7% were treated in a community hospital. The most common diagnosis treated was follicular lymphoma (66.4%), followed by mantle cell lymphoma (16.0%), post-*transplant* lymphoproliferative disorder (2.4%), and other CD 20-positive low-grade lymphomas (15.2%). Indications for *rituximab* *treatment* included failure of previous anthracycline or purine analogue *treatment* in 43.9% of patients and inability to tolerate further chemotherapy in 35.6%. In preliminary data from a subgroup of the cohort, clinical outcomes...
...acquisition costs for this agent for use in the first year were dollar sign1.74 million (US dollars). A state administered central funding structure for *rituximab* results in equitable access throughout a geographically large region.
DESCRIPTORS:
...DISEASES: blood and lymphatic disease, drug *therapy*, immune system disease, neoplastic disease...

...blood and lymphatic disease, drug *therapy*, immune system disease, neoplastic disease...

...blood and lymphatic disease, drug *therapy*, immune system disease, neoplastic disease...

4/3,K/4 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13087280 BIOSIS NO.: 200100294429
NCCTG phase II trial of 2-chlorodeoxyadenosine (2-CDA) as *therapy* for previously treated mantle cell lymphoma: Promising single agent activity limited by brief response duration.
AUTHOR: Inwards David J(a); Fonseca Rafael(a); Kurtin Paul J(a); Habermann Thomas M(a); Knost James; Hillman David W; Witzig Thomas E
AUTHOR ADDRESS: (a)Mayo Clinic, Rochester, MN**USA
JOURNAL: Blood 96 (11 Part 1):p140a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

NCCTG phase II trial of 2-chlorodeoxyadenosine (2-CDA) as *therapy* for previously treated mantle cell lymphoma: Promising single agent activity limited by brief response duration.
...ABSTRACT: characterized by high stage at diagnosis, frequent extranodal sites of involvement, and a poor prognosis. We conducted a phase II trial of 2-CDA for *therapy* of MCL at 5 mg/m2/d IV X 5 days q 28 days for 2-6 cycles depending on response. Cases were stratified according to previous *therapy*. We reported an overall response rate of 81% as initial *therapy* (ASH 1999). This report includes only data from previously treated patients. Central pathology *review* to confirm MCL was required. Twenty-five previously treated patients were enrolled into the study, but 1 was, subsequently deemed ineligible. The remaining 24 included...

...in 4 cases and 5 in 1 case. The median number of previous regimens was 1 (1-6). Previous treatments included: anthracycline-containing regimens (15), *rituximab* (5), platinum-based regimens (1) and autologous stem cell *transplant* (1). Of the 20 patients with available response data from the last previous *therapy*, 11 (55%) had responsive disease. Five patients received 1 cycle, 8 received 2 cycles, 2 received 3 cycles, 4 received 4 cycles, and 5 received...

...for 0-2, 33% for 3-5; p=11). Eleven patients have died to date, 8 from progressive MCL, 1 from infection, 1 from a *transplant*-related complication, and 1 from unknown causes. *Treatment* complications included 1 grade 4 thrombocytopenia, 5 grade 4 neutropenias and 2 grade 4 infections. 2-CDA has significant activity as a single agent for the *treatment* of relapsed mantle cell lymphoma, though responses are of short duration. Subsequent trials will incorporate this active agent in combination with other agents.

4/3,K/5 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

11592261 EMBASE No: 2002162265
Rituximab: Clinical development and future directions
Cheson B.D.
B.D. Cheson, National Cancer Institute, Executive Plaza North, Bethesda, MD 20892 United States
AUTHOR EMAIL: chesonb@ctep.nci.nih.gov
Expert Opinion on Biological Therapy (EXPERT OPIN. BIOL. THER.) (United Kingdom) 2002, 2/1 (97-110)

'CODEN: EOBTA ISSN: 1[redacted]-2598
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 107

The availability of effective monoclonal antibodies (mAbs) has revolutionised the management of patients with B-cell malignancies. The most widely studied of these agents is *rituximab* (Rituxan(TM) IDEC Pharmaceuticals, San Diego, CA), a chimeric anti-CD20 antibody. Using the standard 4-weekly administration schedule, *rituximab* induces responses in almost half of patients with relapsed follicular/low-grade (F/LG) non-Hodgkin's lymphoma (NHL) with complete remissions in 6%. Lower... ...occurrences of a serious syndrome related to cytokine release and rapid tumour clearance. This antibody is also active against aggressive NHL, mantle cell NHL, post-*transplant* lymphoproliferative disorder (PTLD), lymphoplasmacytic NHL and hairy cell leukaemia and is also being evaluated in autoimmune disorders. Combinations of *rituximab* with chemotherapy regimens such as CHOP (cyclophosphamide, adriamycin, vincristine, predinisone) may alter the therapeutic paradigm for these diseases. The future promise of this antibody is...
DRUG DESCRIPTORS:
*rituximab--adverse drug reaction--ae; *rituximab--clinical trial--ct; *rituximab--drug combination--cb; *rituximab--drug comparison--cm; *rituximab--drug dose--do; *rituximab--drug *therapy*--dt; *rituximab--drug toxicity--to; *rituximab--pharmacokinetics--pk; *rituximab--pharmacology--pd
cyclophosphamide--drug combination--cb; cyclophosphamide--drug comparison--cm; cyclophosphamide--drug *therapy*--dt; cyclophosphamide--pharmacology--pd; doxorubicin--drug combination--cb; doxorubicin--drug comparison--cm; doxorubicin--drug *therapy*--dt; doxorubicin--pharmacology--pd; vincristine--drug combination--cb; vincristine--drug comparison--cm; vincristine--drug *therapy*--dt; vincristine--pharmacology--pd; prednisone--drug combination--cb; prednisone--drug comparison--cm; prednisone--drug *therapy*--dt; prednisone--pharmacology--pd; alemtuzumab--drug *therapy*--dt; epratuzumab--drug *therapy*--dt; monoclonal antibody--drug *therapy*--dt; tositumomab i 131--drug *therapy*--dt; ibritumomab tiuxetan--drug *therapy*--dt; tositumomab--drug *therapy*--dt; monoclonal antibody lym 1--drug *therapy*--dt; unclassified drug
MEDICAL DESCRIPTORS:
*nonhodgkin lymphoma--diagnosis--di; *nonhodgkin lymphoma--drug *therapy*--dt; *cancer immunotherapy; *chronic lymphatic leukemia--drug *therapy*--dt
cancer regression; cancer grading; drug tolerability; fever--side effect--si; chill--side effect--si; drug indication; dose response; cytokine release; lymphoproliferative disease--drug *therapy*--dt; cancer classification; human; clinical trial; *review*
DRUG TERMS (UNCONTROLLED): remitogen--drug *therapy*--dt; avastin--drug *therapy*--dt; bevacizumab--drug *therapy*--dt; oncolym--drug *therapy*--dt

4/3,K/6 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

10611858 EMBASE No: 2000078070
Use of rituximab in the *treatment* of lymphoma: An evidence summary
Imrie K.; Esmail R.; Buckstein R.; Berinstein N.; Meyer R.; Zahra H.A.; Chin- Yee I.; Costello B.; Crump M.; De Metz C.; Dhaliwal D.; Gospodarowicz M.; Huebsch L.; Kacsor M.; Kaizer L.; Kouroukis T.; Matthews J.; Meharchand J.; Messner H.; Sawka C.; Smith A.; Walker I.
R. Meyer, Haematology Disease Site Group, Hamilton Regional Cancer Centre, 699 Concession Street, Hamilton, Ont. L8V 5C2 Canada
AUTHOR EMAIL: ralph.meyer@hrcc.on.ca
Current Oncology (CURR. ONCOL.) (Canada) 1999, 6/4 (228-235)
CODEN: CUONF ISSN: 1198-0052
DOCUMENT TYPE: Journal; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 36

Use of rituximab in the *treatment* of lymphoma: An evidence summary

Questions: 1. In what groups of lymphoma patients has *rituximab* been studied? 2. What beneficial *treatment* outcomes are associated with the use of *rituximab* in patients with lymphoma? 3. What is the toxicity of *rituximab*? 4. What patients are more-or-less likely to benefit from *treatment* with *rituximab*?. Perspective: Evidence was selected and reviewed by 2 people, one of whom is a member of the Cancer Care Ontario Practice Guidelines Initiatives Haematology Disease...

...Relevant evidence was identified by a systematic search of the MEDLINE, CANCERLIT, HealthSTAR, CINAHL, PUBMED databases, and the Cochrane Library (using the text words 'rituxan,' '*rituximab*,' 'ritux:,' and 'IDEC C2B8'). Also searched were the American Society of Hematology, the American Society of Clinical Oncology, and the Lugano meeting conference proceedings; the European Organisation for Research and *Treatment* of Cancer and the Physician Data Query databases; and reference lists from selected articles. Patient Population: Patients with non-Hodgkin's lymphoma. Outcomes of Interest...

...and toxicity were the primary outcomes of interest. Results: Search Results: Twenty-eight studies were identified: 1 randomised trial of 2 different dosing strategies for *rituximab* in intermediate-grade lymphoma; 11 reports of single-arm studies of *rituximab* in follicular, low-grade lymphoma, or mantle-cell lymphoma; 1 abstract of a published paper; 8 abstracts of single-arm studies of *rituximab* in low- and intermediate-grade lymphoma, Waldenstrom's macroglobulinaemia, and post-*transplant* lymphoproliferative disorders; 3 abstracts of single-arm studies of *rituximab* in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or interferon alpha in follicular, low- or intermediate-grade lymphoma; 1 paper of a single-arm study of *rituximab* in combination with CHOP in follicular or low- grade lymphoma; 1 abstract of a single-arm study of *rituximab* in combination with fludarabine; 1 abstract of *rituximab* in combination with cyclophosphamide; and 1 abstract of *rituximab* in combination with carmustine (BCNU), cyclophosphamide and etoposide in low-grade or follicular non- Hodgkin's lymphoma. Benefits: The response rates were highest in patients...

...quality of life were not available. Harms: Detailed toxicity data were provided in the published phase II study. The majority of patients (84%) treated with *rituximab* in this study had adverse events. The most common of these were: fever (43%), chills (28%), nausea (18%), headache (14%), and allergic symptoms (43%) including...

...4) toxicity was uncommon. Little haematologic toxicity was noted and there did not appear to be any increase in infections up to 1 year after *therapy*. The majority of adverse events occurred with the first infusion. A 'Dear Doctor' letter was issued indicating that following approval of the drug in the...
...appears more common in patients with high tumour burden or who have more than 50 x 10sup 9 circulating malignant cells per litre. Future Steps: *Rituximab* alone, or in combination with chemotherapy, is being compared with conventional chemotherapy in patients with relapsed, as well as those with newly diagnosed, low-grade or follicular lymphoma. It is also being evaluated as part of initial *therapy* for intermediate-grade lymphoma. At present, the evidence does not allow a firm clinical recommendation on this topic. Please see the full report for a...
DRUG DESCRIPTORS:
*rituximab--adverse drug reaction--ae; *rituximab--clinical trial--ct; *rituximab--drug combination--cb; *rituximab--drug comparison--cm; *rituximab--drug dose--do; *rituximab--drug *therapy*--dt
...reaction--ae; antineoplastic agent--clinical trial--ct; antineoplastic

agent--drug combination- ; antineoplastic agent--drug co[redacted]arison--cm; antineoplastic agent--drug dose--do; antineoplastic agent--drug *therapy* --dt; cyclophosphamide--clinical trial--ct; cyclophosphamide--drug combination--cb; cyclophosphamide--drug comparison--cm; cyclophosphamide --drug *therapy*--dt; doxorubicin--clinical trial--ct; doxorubicin--drug combination--cb; doxorubicin--drug comparison--cm; doxorubicin--drug *therapy*--dt; vincristine--clinical trial--ct; vincristine--drug combination--cb; vincristine--drug comparison--cm; vincristine--drug *therapy*--dt; prednisone--clinical trial--ct; prednisone--drug combination --cb; prednisone--drug comparison--cm; prednisone--drug *therapy*--dt; etoposide--clinical trial--ct; etoposide--drug combination--cb; etoposide --drug comparison--cm; etoposide--drug *therapy*--dt; bleomycin--clinical trial--ct; bleomycin--drug combination--cb; bleomycin--drug comparison--cm; bleomycin--drug *therapy*--dt; fludarabine--clinical trial--ct; fludarabine --drug combination--cb; fludarabine--drug comparison--cm; fludarabine--drug *therapy*--dt; interferon--clinical trial--ct; interferon--drug combination --cb; interferon--drug comparison--cm; interferon--drug *therapy*--dt
MEDICAL DESCRIPTORS:
*lymphoma--drug *therapy*--dt
cancer chemotherapy; cancer immunotherapy; clinical practice; practice guideline; *treatment* outcome; drug induced disease--side effect--si; fever--side effect--si; nausea--side effect--si; headache--side effect--si; cancer survival; quality of life; human; major clinical study; clinical trial; multicenter study; *review*
?ds

Set	Items	Description
S1	266	(ANTI-CD20 OR ANTI-BP35 OR RITUXIMAB) (S) (GRAFT OR TRANSP-LANT OR TRANSLANTATION)
S2	253	S1 AND (TREATMENT OR THERAPY)
S3	133	RD (unique items)
S4	6	S3 AND REVIEW

?s s3 and (in (w) vivo (w) purging)
Processing
Processing
Processing
Processing
Processing

	133	S3
	26770661	IN
	1057283	VIVO
	9024	PURGING
	247	IN(W)VIVO(W)PURGING
S5	17	S3 AND (IN (W) VIVO (W) PURGING)

?t s5/3,k/all

5/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13830763 22322868 PMID: 12435284
Mitoxantrone/Ifosfamide/Etoposide salvage regimen with rituximab for *in* *vivo* *purging* in patients with relapsed lymphoma.
Emmanouilides Christos; Lill Michael; Telatar Milhan; Rosenfelt Fred; Grody Wayne; Territo Mary; Rosen Peter
UCLA Medical School, Division of Hematology/Oncology, Los Angeles, CA.
Clin Lymphoma (United States) Sep 2002.. 3 (2) p111-6, ISSN 1526-9655 Journal Code: 100898741
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

Mitoxantrone/Ifosfamide/Etoposide salvage regimen with rituximab for *in* *vivo* *purging* in patients with relapsed lymphoma.
Treatment with the anti-CD20 antibody *rituximab* prior to stem cell collection may lead to tumor-free stem cell collections in patients with B-cell lymphoma undergoing autologous stem cell transplantation. To...

...collection, 30 patients with a variety of B-cell lymphomas were enrolled in a protocol employing a common MINE (mitoxantrone/ifosfamide/etoposide) salvage regimen with *rituximab* (*in* *vivo* *purging*). *Rituximab* 400 mg/m2 was administered weekly for 3 weeks on days 1, 6, and 8 in relation to the last MINE cycle, which was followed...

...over a median of 5 days. Polymerase chain reaction amplification for the t(14;18) or the heavy-chain gene rearrangement was performed prior to *treatment* and on the leukapheresis sample. Out of 15 patients who had a positive PCR signal prior to *treatment*, 10 had PCR-negative stem cell collections, whereas 5 had PCR-positive stem cell collections. After high-dose chemotherapy and stem cell *transplant*, all patients with a PCR-positive signal pretreatment became PCR negative. We conclude that *rituximab* may increase the yield of tumor-free stem cells. Higher rates of PCR negativity have been reported when more intense and protracted chemoimmunotherapy regimens have been employed. The magnitude of clinical benefit and the significance of the PCR analysis in stem cells after *rituximab* requires larger studies.

5/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13309127 22036397 PMID: 12040531
Improving outcomes in transplantation.
Brugger Wolfram
Eberhard-Karls Universitat, Hamatologie und Onkologie, Medizinische Klinik II, Tubingen, Germany.
Seminars in oncology (United States) Apr 2002, 29 (2 Suppl 6) p23-6, ISSN 0093-7754 Journal Code: 0420432
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Follicular lymphoma and mantle cell lymphoma are incurable with standard chemotherapy regimens. One approach to improve outcome in patients with these diseases is high-dose *therapy* and autologous stem cell transplantation. *Rituximab*, an anti-CD20 monoclonal antibody, is specific for the B-cell surface antigen and can be used in autologous stem cell transplantation to eliminate lymphoma cells before the harvest (*in* *vivo* *purging*) or to prevent regrowth of malignant cells following *transplant* (post-*transplant* *therapy*). Preliminary data from an ongoing multicenter study evaluating the safety and efficacy of *rituximab* as a post-*transplant* consolidation *therapy* in patients with follicular lymphoma and mantle cell lymphoma are presented. After high-dose *therapy* and autologous stem cell transplantation together with *rituximab* *treatment*, 92% of patients are in complete remission at the 18-month study follow-up, suggesting that *rituximab* is a valuable and potentially curative *treatment* for patients with follicular lymphoma and mantle cell lymphoma. Six months after *treatment*, all evaluable patients became polymerase chain reaction-negative for the bcl-1 and bcl-2 chromosomal rearrangements and remained so during follow-up, indicating that *rituximab* is able to eliminate minimal residual disease and bring about high rates of durable remissions in these patients. Copyright 2002, Elsevier Science (USA). All rights...
Descriptors: Antibodies, Monoclonal--therapeutic use--TU; *Antineoplastic Agents--therapeutic use--TU; *Hematopoietic Stem Cell Transplantation; *Lymphoma, Follicular--*therapy*--TH; *Lymphoma, Mantle-Cell--*therapy*--TH; Bone Marrow Purging; Clinical Trials; Combined Modality *Therapy*; Remission Induction; Transplantation, Autologous

5/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13111513 21979733 PMID: 11983102

***In* *vivo* *purging* with rituximab prior to collection of stem cells for autologous transplantation in chronic lymphocytic leukemia.**

Berkahn Leanne; Simpson David; Raptis Anastasios; Klingemann Hans-Georg
Section of Bone Marrow Transplant & Cell Therapy, Rush-Presbyterian-St. Luke's Medical Center, Rush Medical College, Chicago, IL 60612.

Journal of hematotherapy & stem cell research (United States) Apr 2002, 11 (2) p315-20, ISSN 1525-8165 Journal Code: 100892915
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

***In* *vivo* *purging* with rituximab prior to collection of stem cells for autologous transplantation in chronic lymphocytic leukemia.**

Chronic lymphocytic leukemia (CLL) cells express the CD20 antigen, and monoclonal antibodies against CD20 have resulted in remissions. We hypothezised that the anti-CD20 antibody *rituximab* (Rituxantrade mark) may be useful in reducing the number of contaminating CLL cells in stem cell collections for use in autologous transplantation. A pilot study in 5 patients was designed using *rituximab* 375 mg/m(2) as an *in* *vivo* *purging* step following cyclophosphamide 4 gm/m(2) and granulocyte colony-stimulating factor/granulocyte-macrophage colony-stimulating factor (G-CSF/GM-CSF) mobilization *therapy* for patients with advanced-stage CLL undergoing autologous stem cell transplantation. Eligible patients had 0-30% marrow involvement prior to mobilization. A single pre-*rituximab* leukapheresis product was obtained after the white blood cells (WBC) reached 800/mm(3) to serve as a control but was not reinfused. *Rituximab* was administered the following day and subsequent leukaphereses were commenced 48 h later to reach a total of >2 x 10(6) CD34(+) cells/kg...

...the immunoglobulin heavy chain (IgH) were used to evaluate the degree of contaminating CLL cells in the leukapheresis product and to monitor disease status post *transplant*. All 5 patients were informative for the consensus PCR assay. Four of 5 patients mobilized >2 x 10(6) CD34(+) cells/kg and proceeded to...

... All leukaphereses products were positive by PCR for the IgH rearrangement and 4/5 contained CD5/CD19 dual-positive cells. Comparing the pre- and post-*rituximab* leukapheresis products, a reduction in the percentage of CD5(+)/CD19(+) cells was seen in 4/5 patients. All patients engrafted at a median of 13...
... to platelets >20,000/mm(3). No regimen-related mortality was seen. Although 2 patients tested positive on PCR for the IgH rearrangement early after *transplant*, all patients had absence of the IgH gene rearrangement at 1 year and no CD5/CD19 dual-positive cells were could be detected in the bone marrow. This includes 1 heavily pretreated patient who received stem cells containing up to 30% CD5(+)/CD19(+) cells. We conclude that purging with *Rituximab* 48 h prior to stem cell collection was able to reduce significantly (but not eliminate) the percentage of CLL cells in the leukaphereses. However, despite...

... implying that the PCR-positive cells in the leukaphereses may not have long-term clonogenic potential. The results also support the recommendation to test if *rituximab* should be part of a maintenance regimen after *transplant* to prevent disease recurrence in high-risk patients.

5/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12904442 21828527 PMID: 11840154

***In* *vivo* *purging* and relapse prevention following ASCT.**

Gisselbrecht C
Department of Hematology-Oncology, Hopital Saint Louis, Paris, France.

Bone marrow transplant[illegible]on (England) Feb 2002, 29 S[illegible]1 1 pS5-9,
ISSN 0268-3369 Journal Code: 8702459
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

***In* *vivo* *purging* and relapse prevention following ASCT.**

The combination of high-dose chemotherapy and autologous stem cell transplantation (ASCT) is a potentially curative *therapy* for patients with relapsed chemosensitive non-Hodgkin's lymphoma (NHL) and is increasingly being considered as a first-line *treatment* for NHL patients with poor prognosis or poor outcomes from chemotherapy. However, there is a degree of relapse following the latter which is associated with...

... stem cells and/or the presence of residual malignant cells in the host following chemotherapy. Reducing the rate of relapse can be achieved by pre-*transplant* purging of the stem cell *graft* followed by post-*transplant* maintenance to minimise residual disease. Various methods of in vitro purging have been shown to reduce, but not eliminate, the level of stem cell contamination and invariably result in a reduced harvest. To date, this has been reflected in disappointing outcomes for the patient. In contrast, *in* *vivo* *purging* with *rituximab* during the process of stem cell mobilisation and collection does not adversely affect the yield or function of stem cells and shows a significant improvement...

...contamination as measured by bcl-2 clearance. The relapse potential from residual malignant cells in the host can be addressed by a programme of post-*transplant* *rituximab* maintenance *therapy*. In one study 17 patients with follicular lymphoma who underwent ASCT with in vivo *rituximab*-purged stem cells, followed by *rituximab* maintenance, have all remained in complete response at a median follow-up of 12.4 months. The optimum in vivo *rituximab* purging protocol and the precise effect in terms of overall and disease-free survival are currently being evaluated but appear to present an attractive first...

5/3,K/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12904441 21828529 PMID: 11840156

Bcl-2 clearance: optimising outcomes in follicular non-Hodgkin's lymphoma.

Berinstein N L; Buckstein R; Imrie K; Spaner D; Mangel J; Tompkins K; Pennell N; Reis M; Pavlin P; Lima A; Couvadia A; Robinson J; Richardson P
Advanced Therapeutics Program, Toronto-Sunnybrook Regional Cancer Centre and Sunnybrook and Women's College Health Centre, Toronto, Ontario, Canada.
Bone marrow transplantation (England) Feb 2002, 29 Suppl 1 pS14-7,
ISSN 0268-3369 Journal Code: 8702459
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

... such patients and can be detected by polymerase chain reaction (PCR). Complete bcl-2 clearance from the bone marrow (molecular remission) following autologous stem cell *transplant* (ASCT) for follicular NHL is considered to be an important prognostic factor for disease-free survival. Tumour cell contamination of the stem cell grafts used...

... after stem cell collection have been shown to reduce the level of contamination but yield is invariably reduced and grafts remain bcl-2 positive. However, *in* *vivo* *purging* with *rituximab* during the process of collection has been used to obtain bcl-2-negative stem cell harvests without compromising the yield. *Rituximab* is a monoclonal antibody licensed for *treatment* of relapsed and refractory low-grade or

follicular NHL. *Ritux b* targets the CD20 antigen, which is found on cells of the B cell lineage. When used for *in* *vivo* *purging* it depletes the peripheral blood of CD20-positive cells and prevents contamination by lymphoma cells. Molecular remission, as measured by bone-marrow bcl-2 clearance, has been achieved in 7/7 patients with follicular NHL at 1 year after *treatment* with ASCT using *rituximab* as an 'in vivopurse', followed by *rituximab* maintenance. Early clinical outcomes are also encouraging.

5/3,K/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12904439 21828526 PMID: 11840153
Autologous stem cell transplantation in follicular non-Hodgkin's lymphoma.
Pettengell R
Department of Haematology, St George's Hospital Medical School, London, UK.
Bone marrow transplantation (England) Feb 2002, 29 Suppl 1 pS1-4, ISSN 0268-3369 Journal Code: 8702459
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

The failure of conventional chemotherapy to improve overall survival rates in follicular non-Hodgkin's lymphoma (NHL) has led to the development of alternative *treatment* regimens. One such regimen is high-dose chemotherapy (HDT) with autologous stem cell transplantation (ASCT). In ASCT stem cells, harvested predominantly from peripheral blood, are...

... the effect on relapse is unclear. Allogenic stem cell transplants have been associated with a reduced risk of relapse, but this is offset by increased *transplant* -related mortality. The most promising strategy to reduce the rate of relapse following ASCT is *in* *vivo* *purging* using *rituximab*, a monoclonal antibody to CD20. *Rituximab* mobilises mechanisms to kill lymphoma cells, and causes a rapid depletion of B cells from peripheral blood. *Rituximab* has demonstrated good efficacy as monotherapy in patients with both aggressive and indolent lymphoma and has shown very high response rates (>95%) when used in...

5/3,K/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10492051 20023682 PMID: 10561026
Stem cell function and engraftment is not affected by "*in* *vivo* *purging*" with rituximab for autologous stem cell *treatment* for patients with low-grade non-Hodgkin's lymphoma.
Buckstein R; Imrie K; Spaner D; Potichnyj A; Robinson J B; Nanji S; Pennel N; Reis M; Pinkerton P; Dube I; Hewitt K; Berinstein N L
Advanced Therapeutics Program, Toronto Sunnybrook Regional Cancer Center, Sunnybrook Health Sciences Centre, University of Toronto, Ontario.
Seminars in oncology (UNITED STATES) Oct 1999, 26 (5 Suppl 14) p115-22, ISSN 0093-7754 Journal Code: 0420432
Document type: Clinical Trial; Clinical Trial, Phase II; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Stem cell function and engraftment is not affected by "*in* *vivo* *purging*" with rituximab for autologous stem cell *treatment* for patients with low-grade non-Hodgkin's lymphoma.
The chimeric anti-CD20 monoclonal antibody *rituximab* (Rituxan; IDEC Pharmaceuticals, San Diego, CA, and Genentech, Inc, San Francisco, CA) has

recently been approve by the US Food and Drug Administration as single-agent *treatment* of relapsed/refractory low-grade or follicular non-Hodgkin's lymphoma. Initial results from the pivotal clinical trial revealed that response rates to *rituximab* were higher in patients who previously had high-dose *therapy* and autologous stem cell transplantation. We have initiated a clinical trial that combines the use of *rituximab* with high-dose chemotherapy followed by autologous stem cell transplantation for patients with chemosensitive relapsed follicular small cleaved or mantle cell lymphoma. A unique feature of this study is that in addition to eight maintenance infusions of *rituximab* after autologous stem cell transplantation, patients also received *rituximab* 375 mg/m2 2 days before a granulocyte colony-stimulating factor-mobilized stem cell collection as "in vivo purge." We report on preliminary results demonstrating...

... This compares with 11.7 and 11.8 x 10(6)/L, respectively, for the control population. The median CD34 stem cell yield in the *graft* collection was 3.7 x 10(6)/kg in patients receiving *rituximab* in vivo purge compared with 3.1 x 10(6)/kg in the control population. The target stem cell collection was successfully collected in six...

... forming unit-granulocyte monocyte and burst-forming unit-erythrocyte to be 55 and 44 colonies per plate, respectively, for the patients receiving the in vivo *rituximab* purge. This compares favorably with 37 and 38.5 colonies per plate, respectively, for the control population. Neutrophil engraftment took a median of 11 days...

... independence was achieved in 8 days compared with 10 days for the control population. The median number of platelet transfusions was two for patients receiving *rituximab* and 2.5 for the control group. Assessment of serum cytokines immediately before the *rituximab* infusion during the stem cell mobilization and immediately after revealed a twofold to sevenfold increase in interleukin-1beta, tumor necrosis factor-alpha, and interleukin-6...

... minimal residual disease in stem cell collections and in peripheral blood and bone marrow samples of these patients will help to determine the efficacy of *rituximab* in vivo purge on disease progression.

Descriptors: Antibodies, Monoclonal--therapeutic use--TU; *Antineoplastic Agents--therapeutic use--TU; *Hematopoietic Stem Cell Transplantation; *Lymphoma, Low-Grade--*therapy*--TH; *Lymphoma, Mantle-Cell--*therapy*--TH ; Adult; Antigens, CD34; Bone Marrow Purging; Combined Modality *Therapy*; Flow Cytometry; Granulocyte Colony-Stimulating Factor--administration and dosage--AD; Hematopoietic Stem Cell Mobilization; Lymphoma, Low-Grade--drug *therapy*--DT; Lymphoma, Low-Grade--immunology--IM; Lymphoma, Mantle-Cell --drug *therapy*--DT; Lymphoma, Mantle-Cell--immunology--IM; Middle Age; Neoplasm, Residual; Salvage *Therapy*; Transplantation, Autologous

5/3,K/8 (Item 1 from file: 5)

13621298 BIOSIS NO.: 200200250119

Mine-rituxan salvage and *in* *vivo* *purging* in patients with lymphoma.

AUTHOR: Emmanouilides C(a); Lill M; Rosenfelt F; Abdelkedous S(a); Telatar M; Grody W; Territo M(a)
AUTHOR ADDRESS: (a)Hematology/Oncology, UCLA Medical Center, Los Angeles, CA**USA

JOURNAL: Blood 98 (11 Part 1):p738a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

Mine-rituxan salvage and *in* *vivo* *purging* in patients with lymphoma.

...ABSTRACT: tumor-free stem cell collection. Rituxan is an anti-CD20 antibody which preferentially depletes from blood B-cells, thus it is an ideal agent for "*in* *vivo*" *purging*. Due to the potential for synergy with chemotherapy it may enhance the effectiveness of the salvage regimen and due to its long half life it may offer a therapeutic benefit lasting through the high dose *treatment*. We enrolled thirty patients in a protocol employing a common mitoxantrone ifosfamide-etoposide salvage regimen (MINE) with rituxan for salvage and mobilization of stem cells...

...chemotherapy to achieve cytoreduction; stem cells were collected with the administration of 10 mcg/kg of GCSF or 500 mcg GMCSF after the last MINE *treatment*. *Rituximab* was administered at the dose of 400 mg/2 on day-7, 1 and 8 in relation to the last MINE administration. Stem cell collection...

...bcl-2 translocation or clonal immunoglobulin gene rearrangement (nested PCR sensitiveity 1:100,000) was negative in 10 patients and positive in 5. No unusual *transplant* complications were noted. With a median follow up after SCT of 15 months, 4 patients progressed (of which 3 succumbed) while another patient died from *transplant*-related complications. Molecular status of the stem cells did not predict long term outcome. However repeated blood PCR at 3 months after the procedure in...

DESCRIPTORS:

...DISEASES: blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*

5/3,K/9 (Item 2 from file: 5)

13591644 BIOSIS NO.: 200200220465

Autologous stem cell transplants combined with Rituximab for relapsed follicular lymphoma achieve prolonged clinical and molecular remissions.

AUTHOR: Buckstein Rena J(a); Imrie Kevin R(a); Spaner David(a); Mangel Joy (a); Tompkins Kirsty(a); Crump Michael; Coovadia Ahmed(a); Reis Marciano (a); Romans Robert(a); Pennell Nancy(a); Robinson Jean B(a); Hewitt Karen (a); Richardson Pat(a); Lima Ana(a); Pavlin Peggy(a); Boudreau Angela(a); Gitelson Elena(a); Berinstein Neil L(a)
AUTHOR ADDRESS: (a)Advanced Therapeutics Program, Toronto-Sunnybrook Regional Cancer Centre, Sunnybrook and Women's College Health Science Centre, Toronto, ON**Canada

JOURNAL: Blood 98 (11 Part 1):p680a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of

Hematology, Part 1 Orla , Florida, USA December 07-11[redacted]001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Introduction: The benefits of high dose *therapy* in follicular lymphoma are controversial. To maximize response rates and remission durations, we have transplanted patients with relapsed, higher-risk, chemosensitive follicular lymphoma (REAL 1-2) and consolidated with *Rituximab* 375 mg/m2X4 infusions at 2 and 6 months post *transplant* (8 infusions total). The patients also received '*in*-*vivo*' *purging* with a single dose of *Rituximab* 3-5 days prior to stem cell collection. All patients must have achieved 75% reduction tumor bulk and <15% bone marrow positivity to undergo *transplant*. De-bulking chemotherapy was primarily either CHOP (n=9) and/or DHAP (n=14) with a median of 4 cycles given. Conditioning chemotherapy was CBV. Results: Since September 1998, 21 patients have been transplanted in this fashion. No peri-*transplant* mortality occurred. Patients engrafted and became plt transfusion independent at a median of 10 days. No late engraftment failures occurred. With a median follow-up of 23.8 mos overall (range 1.8-33 mos), 1 patient has relapsed at 21 mos post *transplant*, 1 patient has died at 7.2 mos of presumed septic causes. The remainder remain in either CR (n=4) or nCR (n=16). The...

...grade 4), pulmonary aspergillosis (n=2 grade 3), and elevated creatinine (n=1, grade 3). Although grade 2-3 neutropenia was frequently observed during first *Rituximab* infusions post *transplant*, patients were largely asymptomatic. Serial molecular responses by nested PCR of bcl-2 gene rearrangement or V(D)J clonality in PB/BM samples have been obtained in 12/21 of patients. 10/11 stem cell grafts were PCR positive, despite *Rituximab* purging. 9/12 patients became PCR negative at 2 months post *transplant* (pre *Rituximab* course 1) and the 3 patients still positive at this point (2 weakly) all achieved PCR negativity by 6-9 months. 90% of patients were PCR- at 6 months, prior to *Rituximab* course 2. PCR negativity extends to 30+ months post *transplant*. Only one patient has become PCR positive in PB and BM at 24 months, but continues to remain in clinical remission. Conclusions: *Rituximab* immunotherapy as consolidation post high dose *therapy* and stem cell *transplant* for patients with relapsed follicular lymphoma is associated with high rates of durable clinical and molecular remissions. A single infusion of *Rituximab* prior to stem cell harvesting may be insufficient for '*in* *vivo*' *purging* although the clinical significance of *graft* positivity by molecular methods remains unknown. Strategies to eliminate molecular evidence of disease in the stem cell grafts and to combine *Rituximab* with other immunomodulators (ie Interferon) are currently being explored.
DESCRIPTORS:
...DISEASES: blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*

5/3,K/10 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13591630 BIOSIS NO.: 200200220451
Rituximab during autologous stem cell transplantion for lymphoma produces lymphoma free grafts in most patients by PCR and clonogenic assays.
AUTHOR: Flinn Ian W(a); Jones Richard J(a); Goodrich Amy(a); Carter-Brookins Denise(a); Moss Thomas J; Loper Kathy(a); Noga Stephen J (a); Berdeja Jesus G(a); Ambinder Richard F(a)
AUTHOR ADDRESS: (a)Oncology, Johns Hopkins University School of Medicine, Baltimore, MD**USA
JOURNAL: Blood 98 (11 Part 1):p676a-677a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of

Hematology, Part 1 Orla , Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The efficacy of autologous stem cell transplantation for patients with lymphoma is complicated by residual disease remaining in the patient despite the high dose *therapy* and the re-introduction of neoplastic cells with the auto *graft*. We are conducting a trial of *rituximab* used during stem cell mobilization and as a post *transplant* adjuvant in an attempt to overcome both of these obstacles. Tumor contamination of the PBSC *graft* is being measured with lymphoma colony formation and with PCR. Patients with NHL received 375 mg/m2 of *rituximab* day 1 of mobilization, followed by cyclophosphamide 2.5 gm/m2 day 4, GM-CSF 10 ug/kg days 1-7 and G-CSF 10...

...CD 34/kg are collected. The preparative regimen consisted of either cyclophosphamide and total body irradiation or busulfan and cyclophosphamide. GM-CSF is used post-*transplant*. Four weekly doses of *rituximab* are given post-*transplant* 7 days after plts reach 20,000/mm3. Sixty-five patients (45M:20F), median age 52 (range 31-65) have started *therapy*. Diagnoses include 36 follicular center cell, 10 mantle cell, 13 SLL/CLL, 4 marginal zone and 2 Waldenstrom's. Patients had receive a median of 2 (range 1-4) prior therapies. Sixteen patients were in complete remission, 43 in partial remission and 6 in early relapse at time of *transplant*. Fifty-seven of 65 patients were successfully mobilized (median 14.1X106 CD 34/kg, range 2.24X106-60.8X106 CD 34/kg). Fifty-one patients...

...the 57 patients. The number of stem cell grafts free of lymphoma contamination before and after CD34 selection is given. The 4 weekly doses of *rituximab* were generally well tolerated as was, the *therapy* in general. However, several significant unusual late adverse events have been, noted in the day 60 to one year post-*transplant* period including 3 deaths (1 @ day 125 from viral hepatitis, 1 @ day 190 from aspergillosis, and 1 @ day 325 from pseudomonas sepsis), neutropenia, disseminated and...

...infection. With a median follow-up of 195 days, the event-free survival is 82.8% at both 1 and 2 years. We conclude that *in* *vivo* *purging* with *rituximab* and CD34 selection may produce a lymphoma free *graft* in many patients. Further follow-up is required to evaluate a potential for increased late infectious complications.

5/3,K/11 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13528606 BIOSIS NO.: 200200157427
A sequence of immuno-chemotherapy with Rituximab, mobilization of in vivo purged stem cells, high-dose chemotherapy and autotransplant is an effective and nontoxic *treatment* for advanced follicular and mantle cell lymphoma.
AUTHOR: Lazzarino Mario(a); Arcaini Luca(a); Bernasconi Paolo(a); Alessandrino Emilio P(a); Gargantini Livio; Cairoli Roberto; Orlandi Ester(a); Astori Cesare(a); Brusamolino Ercole(a); Pagnucco Guido(a); Colombo Anna A(a); Calatroni Silvia(a); Iacona Isabella; Regazzi Mario B; Morra Enrica
AUTHOR ADDRESS: (a)Division of Hematology, University of Pavia, IRCCS Policlinico San Matteo, Pavia**Italy
JOURNAL: Blood 98 (11 Part 2):p394b November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 2 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971

RECORD TYPE: Abstract
LANGUAGE: English

A sequence of immuno-chemotherapy with Rituximab, mobilization of in vivo purged stem cells, high-dose chemotherapy and autotransplant is an effective and nontoxic *treatment* for advanced follicular and mantle cell lymphoma.

ABSTRACT: Options for relapsed/refractory indolent lymphoma include chemotherapy, immunotherapy, and high-dose *therapy* with autologous progenitor cells support. The best combination of these approaches, however, is not defined. We developed a *treatment* program that combines chemotherapy, immunotherapy, high-dose *therapy* and autotransplant in a sequence of 4 phases, each designed to play a specific role in tumor eradication. This program was applied to 10 patients...

...bcl-2 or bcl-1 rearrangement in blood and marrow achieved a molecular response. Phase 2, immuno-chemotherapy, consisted of two six-day courses with *Rituximab* 375 mg/m2 on day 1, vincristine 2 mg on day 2, and cyclophosphamide 400 mg/m2 from day 2 to day 6. After this...

...bcl-2 or bcl-1 rearrangement showed disappearance of the signal from blood and marrow. The combination was well tolerated with negligible toxicities. Phase 3, *in* *vivo* *purging* and stem cells mobilization, coupled *Rituximab* 375 mg/m2 on day 1 and day 9 with cytarabine 2 g/m2/12h on day 2 and day 3, plus G-CSF from...

...combination was effective in mobilizing an adequate number of progenitor cells that were PCR-negative in all informative cases. Phase 4 consisted of high-dose *therapy* with BEAM followed by rescue with autologous progenitor cells and two doses of *Rituximab* 375 mg/m2 on day 14 and day 21 after *transplant*. Autograft was performed in nine patients. One patient with mantle cell lymphoma progressed pre-*transplant*. The hematopoietic recovery was regular in all cases. The median time to neutrophils over 500 was 12 days, and to platelets over 20,000 was 8 days. After a median follow-up of 10 months (3-15) after *transplant*, all patients are in clinical complete remission. The six patients with molecular marker of disease had persistently negative PCR for bcl-2 or bcl-1 rearrangements in blood and marrow. This sequence of chemotherapy, immuno-chemotherapy, stem cell mobilization with *in* *vivo* *purging*, and autotransplant, organized in 4 blocks of *treatment*, was simple to administer and devoid of toxic effects. It permits rapid attainment of clinical and molecular response and enables the harvest of lymphoma-free ...

DESCRIPTORS:
...DISEASES: blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*

5/3,K/12 (Item 5 from file: 5)

13524421 BIOSIS NO.: 200200153242

Reduced-intensity rituximab-BEAM-CAMPATH allogeneic transplantation for indolent non-Hodgkin's lymphoma.

AUTHOR: Ho Aloysius Y L(a); Devereux Stephen(a); Mufti Ghulam J(a); Pagliuca Antonio(a)
AUTHOR ADDRESS: (a)Department of Haematological Medicine, King's College Hospital, London**UK

JOURNAL: Blood 98 (11 Part 1):p188a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001

ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: standard conditioning regimens. Recently, reduced intensity regimens have significantly reduced early morbidity and mortality and extended the availability of allogeneic HSCT and potential benefits of *graft*-versus-lymphoma (GvL) effects to patients hitherto ineligible. We examine the efficacy of BEAM-CAMPATH (BCNU 300mg/m2 day -6; Cytarabine 200mg/m2 bd days...
...Melphalan 140mg/m2 day -1; CAMPATH-1H 20mg days -5 to -1) as conditioning for allogeneic HSCT in indolent CD20 positive non-Hodgkin's lymphomas. *Rituximab* delivered within 120 days pre-conditioning was used as *in*-*vivo* *purging*. Minimal residual disease was assessed by polymerase chain reaction (pcr) for bcl-2/IgH translocations, and chimerism by X,Y-FISH or pcr amplification of...

...composite follicular-mantle cell lymphoma) with advanced stage (5 Ann Arbour stage IVB, 1 stage IIIA) disease have thus far been recruited (1 without pre-*transplant* *rituximab*). The median age at diagnosis was 48.2 (34.0-52.7) years and at *transplant* 50.9 (34.2-55.8) years. At *transplant*, all were in partial remission after a median of 3 previous courses of chemotherapy (2-7). All initial stage IV patients had continued marrow infiltration...

...of 4.76X106/kg (2.9X106-6.95X106) and 1 bone marrow from a volunteer-unrelated donor with 3.45X106/kg CD34+ cells. Immediate post-*transplant* morbidity was limited to NCIC grade 1-2 stomatitis; nausea/vomiting, and grade 3 febrile neutropenia. Neutrophil (>0.5X109/1) and platelet (>20X109/1) regeneration occurred at medians of 12.5 (11-29) and 12.0 (10-50) days respectively. Grade II skin and liver *graft* -versus-host disease (GvHD) occurred in 1 patient and limited chronic GvHD in another (D+129). All were alive at a median follow-up of 190.5 (105-385) days with ECOG performance status 0-1. Clinical and radiological complete remission following *transplant* continued in 4 patients with 2 demonstrating very weak pcr positivity and 1 persistently negativity. Progressive disease occurred in 2 patients. Both were strongly pcr positive following *transplant*. One developed rapidly progressive nodal disease at D+80, the other radiological evidence of slowly progressive nodal disease at D+99. Both failed to respond nodally to post-*transplant* *rituximab* although the former became pcr negative and had morphological clearance of marrow. Donor lymphocyte infusion (DLI) resulted in regression of nodal disease and re-establishment of predominant donor chimerism. Although follow-up is short, reduced intensity allogeneic HSCT with BEAM-CAMPATH conditioning appears to be safe and potentially curative. A *graft* versus lymphoma effect is demonstrable. Further investigation is required into the role of *Rituximab* in this setting, and into any potential anti-lymphoma properties of CAMPATH. Improved sensitivity in quantitative MRD methodology may allow better accuracy in scheduling *rituximab* and/or DLI in the post-HSCT setting.
DESCRIPTORS:
...DISEASES: blood and lymphatic disease, immune system disease, neoplastic disease, pathology, *therapy*;

5/3,K/13 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13524039 BIOSIS NO.: 200200152860
Unexpected toxicities of combined rituximab and GM-CSF in autologous transplants for CD20 positive lymphoma.
AUTHOR: Ehmann W Christopher(a); Mierski Joseph A(a); Claxton David F(a); Rybka Witold B(a)
AUTHOR ADDRESS: (a)Hematology/Oncology, Pennsylvania State University

College of Medicine, H[redacted]shey, PA**USA
JOURNAL: Blood 98 (11 Part 2):p345b-346b November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 2 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In an effort to prolong disease-free survival in patients with CD20+ lymphomas, a protocol utilizing *rituximab* for *in* *vivo* *purging* and prolonged administration of GM-CSF for increasing dendritic cell differentiation was initiated. In this study, patients are mobilized with cyclophosphamide (5grams/m2) and etoposide (1gram/m2) followed by *rituximab* (375mg/m2) weeklyX4 and GM-CSF 250mg/m2 day until completion of stem cell collection. Transplantation conditioning consists of busulfan 0.8mg/kg IVX16 doses and cyclophosphamide 120mg/kg in two divided doses. *Rituximab* (375mg/m2) is administered for four weekly doses beginning on day 0 and GM-CSF is given at 250mg/m2 daily beginning day+1 until day+30 post-*transplant*. Primary endpoints of this study are the ability to mobilize an adequate number of stem cells (gtoreq2.0X106 CD34+ cells/kg recipient weight) and time...

...G-CSF (5 mug/kg) and the same conditioning (except for busulfan given orally, 1mg/kgX16 doses) with G-CSF given until granulocyte recovery. No *rituximab* was included in the *therapy* of these previously treated patients. To date, ten patients have been treated on this study. For the entire group, two failed to mobilize and times...

...12 days. The 80% mobilization rate and times to engraftment of granulocytes and platelets matched our prior experience for patients with lymphoma who underwent autologous *transplant*. Although the primary endpoints showed no deleterious effects of this new *treatment*, the first four patients treated on this study had unexpected toxicities with late cytopenias and a high incidence of infections: Patient 1 had engraftment of...
...an episode of gram positive bacteremia. With resolution of her infection, her platelet count rose to normal. Patient 3 recovered his platelet count early post-*transplant* but developed gram-negative sepsis with profound thrombocytopenia; his platelet count then gradually rose to normal as his infection resolved. Patient 4 engrafted normally but...

...161. Because of the unexpected toxicities encounted by these first four patients the protocol was amended. The next 6 patients enrolled received no ritaximab post-*transplant* and GM-CSF was administered only until the ANC increased to gtoreq500/mm3 for 2 consecutive days post-*transplant*. Of the six patients treated on the revised protocol, two failed to mobilize, four went on to *transplant*. Only one of the four patients who underwent transplantation had late unexplained transient pancytopenia without clinical sequelae, and none had infections. Thus, the excess toxicity seen in the first four patients is attributable to the post-*transplant* *rituximab* and prolonged GM-CSF *therapy*. Additional studies on the effects of combined *rituximab*/GM-CSF *therapy* on molecular purging and dendritic cell number and function are underway.

5/3,K/14 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13523806 BIOSIS NO.: 200200152627
Effectiveness of Mabthera in advanced stages B-CLL and for *in* *vivo* *purging* autologous peripheral stem cell transplantation.
AUTHOR: Shtalrid Mordechai(a); Shvidel Lev(a); Klepfish Abraham(a); Haran Michal(a); Berrebi Alain(a)
AUTHOR ADDRESS: (a)Hematology Institute, Kaplan Medical Center, Rehovot**

Israel
JOURNAL: Blood 98 (11 Part 2):p293b November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 2 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

Effectiveness of Mabthera in advanced stages B-CLL and for *in* *vivo* *purging* autologous peripheral stem cell transplantation.

ABSTRACT: Mabthera (*Rituximab*, Roche) a chimeric monoclonal antibody directed against CD20 molecule, has been found effective in *treatment* of low grade lymphoma. The use of Mabthera in CLL is still controversial because of low expression of CD20 antigen on CLL cell comparing to...

...and 2 with de novo PLL. All but 2 were heavily previously treated, 4 of them relapsing after APSCT. Mabthera was given either as salvage *therapy* in 6 patients who were refractory to chemotherapy, or to eradicate minimal residual disease (MRD) in chemosensitive patients before harvesting of PSC (7 patients). Four...

...after Mabthera administration. In the second group of chemoresponsive patients treated with Mabthera, 6 entered in complete remission and one in good PR allowing an *in* *vivo* *purging* of the harvest. Three were autografted and retreated with Mabthera post-*transplant*, two remained in CR for 6 and 15 months, one developed a mild B cell clone 12 months after *transplant*. In conclusion, Mabthera is effective in chemosensitive CLL improving the quality of response and allowing *in* *vivo* *purging* before stem cell harvesting. Two PLL patients responded to combination of chemotherapy and Mabthera and achieved CR.
DESCRIPTORS:
...DISEASES: blood and lymphatic disease, drug *therapy*, immune system disease, neoplastic disease, surgery

5/3,K/15 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13501181 BIOSIS NO.: 200200130002
Molecular response to anti Cd20 (Rituximab) *therapy* in relapsed follicular lymphoma.
AUTHOR: Giraldo Pilar(a); Pelegrin Fatima; Palomera Luis(a); Recasens Valle (a); Najera Maria J(a); Perdiguer Luis(a); Puente Fernando(a); Rubio-Felix Daniel(a)
AUTHOR ADDRESS: (a)Hematology, SAHH Cooperative Study Group, Zaragoza** Spain
JOURNAL: Blood 98 (11 Part 1):p135a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

Molecular response to anti Cd20 (Rituximab) *therapy* in relapsed follicular lymphoma.

...ABSTRACT: gene translocation is related with frequent relapses. Purpose: To determine the efficacy of a Fludarabine-Mitoxantrone regimen (FLD/MTX) combined with monoclonal anti CD20 antibody (*Rituximab*) to induce clinical and molecular response in patients with relapsed follicular lymphoma (FL). Patients and methods: A prospective trial was conduced in 30 consecutive patients...

...Therapeutic schedule: FLD 30 mg/m2 days 1 to 3 and MTX 10 mg/m2 day 1, were administered monthtly for 4 months followed by *Rituximab* (375 mg/m2/weekly X4). Inclusion criteria: relapsed FL nodal biopsy with Bcl-2 immunohistochemistry expression, ECOG<3, normal liver and renal function, no concomitant diseases. Both clinical and molecular response were evaluated: PCR-ELISA assay for t(14;18) in peripheral blood (PB) and bone marrow (BM), prior to *therapy*, after FLD-MTX and two months after *Rituximab* *treatment* was completed. Results: mean age: 56.00+-12.44 (range 32-77); M/F: 12/18. ECOG: 0(22), 1(5), 2(2), 3(1...

...Response: 20 cases (66.6%) were valuable for response after FLD-MTX, showing 16 (80.0%) complete (CR-7) or partial response (PR-9). After *Rituximab* *therapy* (16 patients) the response rates were: CR-9 (56.3%) or PR-5 (31.2%) and 2 failures (12.5%), in 7 patients with CR an autologous stem cell *transplant* were performed. Molecular response: from 22 cases with positive BM t(14;18), 14 (63.6%) achieved molecular response, one after FLD-MTX. The median RFS of the group is 23 months. After 24 months of follow-up 79% are alive. Comments: FLD-MTX *therapy* induces clinical response in 80% of relapsed FL patients, with CR rates of 35.0%. *Rituximab* *therapy* does not influence but improves CR rates (56.3%). Furthermore it is capable to obtain *in* *vivo* *purging* in 77.2% of cases. In our opinion combined FLD-MTX chemotherapy plus *Rituximab* could be a good therapeutic scheme previously to stem-cell harvesting.

DESCRIPTORS:

...DISEASES: blood and lymphatic disease, drug *therapy*, immune system disease, neoplastic disease

5/3,K/16 (Item 9 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

13110044 BIOSIS NO.: 200100317193

Primary autologous stem cell transplantation in mantle cell lymphoma: Clinical and molecular response.

AUTHOR: Geisler Christian H(a); Elonen Erkki; Johnson Anna; Kolstad Arne; Andersen N S(a)

AUTHOR ADDRESS: (a)Hematology, Rigshospitalet, Copenhagen**Denmark

JOURNAL: Blood 96 (11 Part 1):p794a-795a November 16, 2000

MEDIUM: print

CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000

SPONSOR: American Society of Hematology

ISSN: 0006-4971

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

...ABSTRACT: for molecular response, 6 were PCR-negative. Of these one has relapsed. Stem-cell Purging: Methods used were mainly CD34+ cell selection (12 pts) or *in*-*vivo* *purging* with *Rituximab* 375 mg/m2 single infusion (4 pts). By a quantitative RT-PCR against the available clonal marker, the mean absolute No.s of tumor cells (TC) X 106 given back to the patients at *transplant* were as follows: In 7 unpurged cases 37 (range 3-60), in 12 CD34+ cell selected cases 1.7 (3-60) and in 4 in-vivo purged cases 13.3 (5-30). Conclusions: Primary *treatment* with high-dose *therapy* and autologous stem cell transplantation in MCL is promising, but a significant proportion fails *treatment* before reaching *transplant*. Molecular remission is possible, but the clinical significance is not yet known. A significant No. of tumor cells are given back, which can be reduced one log by CD34' cell selection. A revised Nordic MCL protocol with intensified induction *treatment* and purging efforts is now being activated.

```
### Status: Path 1 of [Dialog Information Services via Modem]

### Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSSS?
### Status: Signing onto Dialog
 ********
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
### Status: Connected


Dialog level 02.12.20D

Last logoff:  23dec02 11:47:01
Logon file001 23dec02 13:17:06
KWIC is set to 50.
HILIGHT set on as '*'
* **                                  **

File   1:ERIC  1966-2002/Dec 13
       (c) format only 2002 The Dialog Corporation

      Set  Items  Description
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Cost is in DialUnits
?b 155, 159, 5, 55
       23dec02 13:17:20 User259876 Session D448.1
            $0.29    0.084 DialUnits File1
     $0.29  Estimated cost File1
     $0.04  TELNET
     $0.33  Estimated cost this search
     $0.33  Estimated total session cost   0.084 DialUnits


SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2002/Nov W3
*File 155: For updating information please see Help News155. Alert
feature enhanced with customized scheduling. See HELP ALERT.
  File 159:Cancerlit  1975-2002/Oct
        (c) format only 2002 Dialog Corporation
  File   5:Biosis Previews(R)  1969-2002/Dec W3
        (c) 2002 BIOSIS
*File   5: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File  55:Biosis Previews(R)  1993-2002/Dec W3
        (c) 2002 BIOSIS
*File  55: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.

      Set  Items  Description
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?s (anti-CD20 or anti-Bp35 or Rituximab) (s) (graft or transplant or transplantation)
              30  ANTI-CD20
               0  ANTI-BP35
            2746  RITUXIMAB
          271177  GRAFT
          153261  TRANSPLANT
          620399  TRANSPLANTATION
     S1      508  (ANTI-CD20 OR ANTI-BP35 OR RITUXIMAB) (S) (GRAFT OR
                  TRANSPLANT OR TRANSPLANTATION)
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?s s1 and (treatment or therapy)
             508  S1
         3607917  TREATMENT
         3194308  THERAPY
      S2     477  S1 AND (TREATMENT OR THERAPY)
?rd
...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...examined 50 records  (200)
...examined 50 records  (250)
...examined 50 records  (300)
...examined 50 records  (350)
...examined 50 records  (400)
...examined 50 records  (450)
...completed examining records
      S3     199  RD (unique items)
?s s3 and (in (w) vivo (w) purging)
Processing
Processing
Processing
Processing
             199  S3
        23814642  IN
          950840  VIVO
            8325  PURGING
             269  IN(W)VIVO(W)PURGING
      S4      24  S3 AND (IN (W) VIVO (W) PURGING)
?t s4/3,k/all
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4/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13830763 22322868 PMID: 12435284

Mitoxantrone/Ifosfamide/Etoposide salvage regimen with rituximab for *in* *vivo* *purging* in patients with relapsed lymphoma.

Emmanouilides Christos; Lill Michael; Telatar Milhan; Rosenfelt Fred; Grody Wayne; Territo Mary; Rosen Peter
UCLA Medical School, Division of Hematology/Oncology, Los Angeles, CA.

Clin Lymphoma (United States) Sep 2002, 3 (2) p111-6, ISSN 1526-9655 Journal Code: 100898741
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

Mitoxantrone/Ifosfamide/Etoposide salvage regimen with rituximab for *in* *vivo* *purging* in patients with relapsed lymphoma.

Treatment with the anti-CD20 antibody *rituximab* prior to stem cell collection may lead to tumor-free stem cell collections in patients with B-cell lymphoma undergoing autologous stem cell *transplantation*. To test the feasibility of obtaining polymerase chain reaction (PCR)-negative stem cell collection, 30 patients with a variety of B-cell lymphomas were enrolled in a protocol employing a common MINE (mitoxantrone/ifosfamide/etoposide) salvage regimen with *rituximab* (*in* *vivo* *purging*). *Rituximab* 400 mg/m2 was administered weekly for 3 weeks on days 1, 6, and 8 in relation to the last MINE cycle, which was followed...

...over a median of 5 days. Polymerase chain reaction amplification for the t(14;18) or the heavy-chain gene rearrangement was performed prior to *treatment* and on the leukapheresis sample. Out of 15 patients who had a positive PCR signal prior to *treatment*, 10 had PCR-negative stem cell collections, whereas 5 had PCR-positive stem cell collections. After high-dose chemotherapy and stem cell *transplant*, all patients with a PCR-positive signal pretreatment became PCR negative. We conclude that

rituximab may increase the yield of tumor-free stem cells. Higher rates of PCR negativity have been reported when more intense and protracted chemoimmunotherapy regimens have been employed. The magnitude of clinical benefit and the significance of the PCR analysis in stem cells after *rituximab* requires larger studies.

4/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13309127 22036397 PMID: 12040531
Improving outcomes in transplantation.
Brugger Wolfram
Eberhard-Karls Universitat, Hamatologie und Onkologie, Medizinische Klinik II, Tubingen, Germany.
Seminars in oncology (United States) Apr 2002, 29 (2 Suppl 6) p23-6, ISSN 0093-7754 Journal Code: 0420432
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Follicular lymphoma and mantle cell lymphoma are incurable with standard chemotherapy regimens. One approach to improve outcome in patients with these diseases is high-dose *therapy* and autologous stem cell *transplantation*. *Rituximab* , an anti-CD20 monoclonal antibody, is specific for the B-cell surface antigen and can be used in autologous stem cell *transplantation* to eliminate lymphoma cells before the harvest (*in* *vivo* *purging*) or to prevent regrowth of malignant cells following *transplant* (post-*transplant* *therapy*). Preliminary data from an ongoing multicenter study evaluating the safety and efficacy of *rituximab* as a post-*transplant* consolidation *therapy* in patients with follicular lymphoma and mantle cell lymphoma are presented. After high-dose *therapy* and autologous stem cell *transplantation* together with *rituximab* *treatment* , 92% of patients are in complete remission at the 18-month study follow-up, suggesting that *rituximab* is a valuable and potentially curative *treatment* for patients with follicular lymphoma and mantle cell lymphoma. Six months after *treatment* , all evaluable patients became polymerase chain reaction-negative for the bcl-1 and bcl-2 chromosomal rearrangements and remained so during follow-up, indicating that *rituximab* is able to eliminate minimal residual disease and bring about high rates of durable remissions in these patients. Copyright 2002, Elsevier Science (USA). All rights...
Descriptors: Antibodies, Monoclonal--therapeutic use--TU; *Antineoplastic Agents--therapeutic use--TU; *Hematopoietic Stem Cell Transplantation; *Lymphoma, Follicular--*therapy*--TH; *Lymphoma, Mantle-Cell--*therapy*--TH ; Bone Marrow Purging; Clinical Trials; Combined Modality *Therapy*; Remission Induction; Transplantation, Autologous

4/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13224418 22040160 PMID: 12044225
In vitro and *in* *vivo* *purging* of B lymphoma cells from stem-cell products using anti-CD20 Abs.
Derigs
Cytotherapy (England) 2000, 2 (6) p445-53, ISSN 1465-3249 Journal Code: 100895309
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

In vitro and *in* *vivo* *purging* of B lymphoma cells from stem-cell products using anti-CD20 Abs.

BACKGROUND: Autologous stem-cell *transplantation* has proved curative *therapy* for relapsed NHL. However, recurrence of underlying disease remains the major cause of *treatment* failure in this setting. METHODS: Development of effective MAb *therapy* directed against the B cell surface antigen CD20 has added a valuable tool of clearing contaminating lymphoma cells from stem-cell products by either in vitro or in vivo application. RESULTS: *Transplantation* of successfully in vitro purged bone marrow using Mabs has been correlated with prolonged survival in large Phase-II study. So far, no randomized trial could demonstrate a therapeutic benefit for in vitro purging. The anti-CD20 Mab *rituximab* has been used for *in* *vivo* *purging* at the time of stem cell collection or peritransplantation. This method has been shown to be safe and feasable. In the majority of patients the combination of *rituximab* with anti-lymphoma chemotherapy meant the collected stem cell products were free of molecularly-detectable lymphoma cells. DISCUSSION: The increasing ability to kill all lymphoma cells in vivo by regimens including myeloablative *therapy* renders contaminating lymphoma cells of the autologous stem cell product the main source for desease recurrence. Clearing of these cells remains a prerequisite for curative stem-cell *transplantation* . Establishment of safe and effective therapeutic schedules using Mabs will enhance the chance for collection of lymphoma-free hematopoietic stems cells.

4/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13217524 22035147 PMID: 12040475
***Rituximab* *in* *vivo* *purging* is safe and effective in combination with CD34-positive selected autologous stem cell *transplantation* for salvage *therapy* in B-NHL.**
Flohr T; Hess G; Kolbe K; Gamm H; Nolte H; Stanislawski T; Huber C; Derigs H G
IIIrd Department of Medicine, Johannes Gutenberg-University, Mainz and Hospital Kemperhof, Koblenz, Germany.
Bone marrow transplantation (England) May 2002, 29 (9) p769-75, ISSN 0268-3369 Journal Code: 8702459
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

***Rituximab* *in* *vivo* *purging* is safe and effective in combination with CD34-positive selected autologous stem cell *transplantation* for salvage *therapy* in B-NHL.**
... mobilization. Additional ex vivo selection of CD34-positive cells was performed using the CliniMacs device. Two doses of Rituximab were included in the high-dose *therapy* regimen (HDT). R-DexaBEAM was well tolerated and 26 of 27 patients mobilized sufficient numbers of CD34(+) blood stem cells. Application of R-DexaBEAM resulted in significant depletion of peripheral B cells. No *treatment* -related deaths occurred after HDT and all patients showed stable engraftment of hematopoesis. Combined immunodeficiency was observed post HDT and eight patients developed CMV antigenemia...

... With regard to histology, PFS was 71% in aggressive lymphoma (n = 11), 74% in indolent FCL (n = 10) and 100% in MCL (n = 5). The *treatment* protocol has proven feasible, with high purging efficiency and encouraging remission rates.

4/3,K/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13111513 21979733 PMID: 11983102
***In* *vivo* *purging* with *rituximab* prior to collection of stem cells for autologous *transplantation* in chronic lymphocytic leukemia.**

Berkahn Leanne; Simpson David; Raptis Anastasios; Klinge Hahn Hans-Georg
Section of Bone Marrow Transplant & Cell Therapy, Rush-Presbyterian-St. Luke's Medical Center, Rush Medical College, Chicago, IL 60612.
Journal of hematotherapy & stem cell research (United States) Apr 2002, 11 (2) p315-20, ISSN 1525-8165 Journal Code: 100892915
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

***In* *vivo* *purging* with *rituximab* prior to collection of stem cells for autologous *transplantation* in chronic lymphocytic leukemia.**

Chronic lymphocytic leukemia (CLL) cells express the CD20 antigen, and monoclonal antibodies against CD20 have resulted in remissions. We hypothezised that the anti-CD20 antibody *rituximab* (Rituxantrade mark) may be useful in reducing the number of contaminating CLL cells in stem cell collections for use in autologous *transplantation*. A pilot study in 5 patients was designed using *rituximab* 375 mg/m(2) as an *in* *vivo* *purging* step following cyclophosphamide 4 gm/m(2) and granulocyte colony-stimulating factor/granulocyte-macrophage colony-stimulating factor (G-CSF/GM-CSF) mobilization *therapy* for patients with advanced-stage CLL undergoing autologous stem cell *transplantation*. Eligible patients had 0-30% marrow involvement prior to mobilization. A single pre-*rituximab* leukapheresis product was obtained after the white blood cells (WBC) reached 800/mm(3) to serve as a control but was not reinfused. *Rituximab* was administered the following day and subsequent leukaphereses were commenced 48 h later to reach a total of >2 x 10(6) CD34(+) cells/kg...

...the immunoglobulin heavy chain (IgH) were used to evaluate the degree of contaminating CLL cells in the leukapheresis product and to monitor disease status post *transplant*. All 5 patients were informative for the consensus PCR assay. Four of 5 patients mobilized >2 x 10(6) CD34(+) cells/kg and proceeded to...

... All leukaphereses products were positive by PCR for the IgH rearrangement and 4/5 contained CD5/CD19 dual-positive cells. Comparing the pre- and post-*rituximab* leukapheresis products, a reduction in the percentage of CD5(+)/CD19(+) cells was seen in 4/5 patients. All patients engrafted at a median of 13...
... to platelets >20,000/mm(3). No regimen-related mortality was seen. Although 2 patients tested positive on PCR for the IgH rearrangement early after *transplant*, all patients had absence of the IgH gene rearrangement at 1 year and no CD5/CD19 dual-positive cells were could be detected in the bone marrow. This includes 1 heavily pretreated patient who received stem cells containing up to 30% CD5(+)/CD19(+) cells. We conclude that purging with *Rituximab* 48 h prior to stem cell collection was able to reduce significantly (but not eliminate) the percentage of CLL cells in the leukaphereses. However, despite...

... implying that the PCR-positive cells in the leukaphereses may not have long-term clonogenic potential. The results also support the recommendation to test if *rituximab* should be part of a maintenance regimen after *transplant* to prevent disease recurrence in high-risk patients.

4/3,K/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12904442 21828527 PMID: 11840154
***In* *vivo* *purging* and relapse prevention following ASCT.**
Gisselbrecht C
Department of Hematology-Oncology, Hopital Saint Louis, Paris, France.
Bone marrow transplantation (England) Feb 2002, 29 Suppl 1 pS5-9, ISSN 0268-3369 Journal Code: 8702459
Document type: Journal Article
Languages: ENGLISH

Main Citation Owner: N[redacted]
Record type: In Process

***In* *vivo* *purging* and relapse prevention following ASCT.**

The combination of high-dose chemotherapy and autologous stem cell *transplantation* (ASCT) is a potentially curative *therapy* for patients with relapsed chemosensitive non-Hodgkin's lymphoma (NHL) and is increasingly being considered as a first-line *treatment* for NHL patients with poor prognosis or poor outcomes from chemotherapy. However, there is a degree of relapse following the latter which is associated with...

... stem cells and/or the presence of residual malignant cells in the host following chemotherapy. Reducing the rate of relapse can be achieved by pre-*transplant* purging of the stem cell *graft* followed by post-*transplant* maintenance to minimise residual disease. Various methods of in vitro purging have been shown to reduce, but not eliminate, the level of stem cell contamination and invariably result in a reduced harvest. To date, this has been reflected in disappointing outcomes for the patient. In contrast, *in* *vivo* *purging* with *rituximab* during the process of stem cell mobilisation and collection does not adversely affect the yield or function of stem cells and shows a significant improvement...

...contamination as measured by bcl-2 clearance. The relapse potential from residual malignant cells in the host can be addressed by a programme of post-*transplant* *rituximab* maintenance *therapy* . In one study 17 patients with follicular lymphoma who underwent ASCT with in vivo *rituximab*-purged stem cells, followed by *rituximab* maintenance, have all remained in complete response at a median follow-up of 12.4 months. The optimum in vivo *rituximab* purging protocol and the precise effect in terms of overall and disease-free survival are currently being evaluated but appear to present an attractive first...

4/3,K/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12904441 21828529 PMID: 11840156

Bcl-2 clearance: optimising outcomes in follicular non-Hodgkin's lymphoma.

Berinstein N L; Buckstein R; Imrie K; Spaner D; Mangel J; Tompkins K; Pennell N; Reis M; Pavlin P; Lima A; Couvadia A; Robinson J; Richardson P
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Bone marrow transplantation (England) Feb 2002, 29 Suppl 1 pS14-7, ISSN 0268-3369 Journal Code: 8702459
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

... such patients and can be detected by polymerase chain reaction (PCR). Complete bcl-2 clearance from the bone marrow (molecular remission) following autologous stem cell *transplant* (ASCT) for follicular NHL is considered to be an important prognostic factor for disease-free survival. Tumour cell contamination of the stem cell grafts used in ASCT is commonly associated with relapse. This can be addressed by purging the stem cell harvest prior to *transplantation* . Various methods of in vitro purging after stem cell collection have been shown to reduce the level of contamination but yield is invariably reduced and grafts remain bcl-2 positive. However, *in* *vivo* *purging* with *rituximab* during the process of collection has been used to obtain bcl-2-negative stem cell harvests without compromising the yield. *Rituximab* is a monoclonal antibody licensed for *treatment* of relapsed and refractory low-grade or follicular NHL. *Rituximab* targets the CD20 antigen, which is found on cells of the B cell lineage. When used for *in* *vivo* *purging* it depletes the peripheral blood of CD20-positive cells and prevents

Cell Transplantation; *Immunotherapy; *Lymphoma, Non-Hodgkin--*therapy*--TH ; Adult; Aged; Antibodies, Monoclonal--immunology--IM; Antineoplastic Agents--immunology--IM; Bone Marrow Purging; Combined Modality *Therapy*; Lymphoma, Non-Hodgkin--immunology--IM; Middle Age; Transplantation, Autologous; *Treatment* Outcome

4/3,K/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10492051 20023682 PMID: 10561026

Stem cell function and engraftment is not affected by "*in* *vivo* *purging*" with rituximab for autologous stem cell *treatment* for patients with low-grade non-Hodgkin's lymphoma.

Buckstein R; Imrie K; Spaner D; Potichnyj A; Robinson J B; Nanji S; Pennel N; Reis M; Pinkerton P; Dube I; Hewitt K; Berinstein N L
Advanced Therapeutics Program, Toronto Sunnybrook Regional Cancer Center, Sunnybrook Health Sciences Centre, University of Toronto, Ontario.
Seminars in oncology (UNITED STATES) Oct 1999, 26 (5 Suppl 14) p115-22, ISSN 0093-7754 Journal Code: 0420432
Document type: Clinical Trial; Clinical Trial, Phase II; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Stem cell function and engraftment is not affected by "*in* *vivo* *purging*" with rituximab for autologous stem cell *treatment* for patients with low-grade non-Hodgkin's lymphoma.

The chimeric anti-CD20 monoclonal antibody *rituximab* (Rituxan; IDEC Pharmaceuticals, San Diego, CA, and Genentech, Inc, San Francisco, CA) has recently been approved by the US Food and Drug Administration as single-agent *treatment* of relapsed/refractory low-grade or follicular non-Hodgkin's lymphoma. Initial results from the pivotal clinical trial revealed that response rates to *rituximab* were higher in patients who previously had high-dose *therapy* and autologous stem cell *transplantation*. We have initiated a clinical trial that combines the use of *rituximab* with high-dose chemotherapy followed by autologous stem cell *transplantation* for patients with chemosensitive relapsed follicular small cleaved or mantle cell lymphoma. A unique feature of this study is that in addition to eight maintenance infusions of *rituximab* after autologous stem cell *transplantation*, patients also received *rituximab* 375 mg/m2 2 days before a granulocyte colony-stimulating factor-mobilized stem cell collection as "in vivo purge." We report on preliminary results demonstrating the safety and efficacy of the in vivo purge on 10 patients undergoing stem cell mobilization, nine of whom have already undergone *transplantation* . The peripheral blood CD34+ counts were 14.92 and 20 x 10(6)/L on day 4 and day 5, respectively, of the stem cell...

... This compares with 11.7 and 11.8 x 10(6)/L, respectively, for the control population. The median CD34 stem cell yield in the *graft* collection was 3.7 x 10(6)/kg in patients receiving *rituximab* in vivo purge compared with 3.1 x 10(6)/kg in the control population. The target stem cell collection was successfully collected in six...
... forming unit-granulocyte monocyte and burst-forming unit-erythrocyte to be 55 and 44 colonies per plate, respectively, for the patients receiving the in vivo *rituximab* purge. This compares favorably with 37 and 38.5 colonies per plate, respectively, for the control population. Neutrophil engraftment took a median of 11 days...

... independence was achieved in 8 days compared with 10 days for the control population. The median number of platelet transfusions was two for patients receiving *rituximab* and 2.5 for the control group. Assessment of serum cytokines immediately before the *rituximab* infusion during the stem cell mobilization and immediately after revealed a twofold to sevenfold increase in interleukin-1beta, tumor necrosis factor-alpha, and interleukin-6...

... minimal residual disease in stem cell collections and in peripheral blood and bone marrow samples of these patients will help to determine the efficacy of *rituximab* in vivo purge on disease progression.
Descriptors: Antibodies, Monoclonal--therapeutic use--TU; *Antineoplastic Agents--therapeutic use--TU; *Hematopoietic Stem Cell Transplantation; *Lymphoma, Low-Grade--*therapy*--TH; *Lymphoma, Mantle-Cell--*therapy*--TH ; Adult; Antigens, CD34; Bone Marrow Purging; Combined Modality *Therapy*; Flow Cytometry; Granulocyte Colony-Stimulating Factor--administration and dosage--AD; Hematopoietic Stem Cell Mobilization; Lymphoma, Low-Grade--drug *therapy*--DT; Lymphoma, Low-Grade--immunology--IM; Lymphoma, Mantle-Cell --drug *therapy*--DT; Lymphoma, Mantle-Cell--immunology--IM; Middle Age; Neoplasm, Residual; Salvage *Therapy*; Transplantation, Autologous

4/3,K/12 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13621298 BIOSIS NO.: 200200250119
Mine-rituxan salvage and *in* *vivo* *purging* in patients with lymphoma.
AUTHOR: Emmanouilides C(a); Lill M; Rosenfelt F; Abdelkedous S(a); Telatar M; Grody W; Territo M(a)
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JOURNAL: Blood 98 (11 Part 1):p738a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

Mine-rituxan salvage and *in* *vivo* *purging* in patients with lymphoma.

...ABSTRACT: tumor-free stem cell collection. Rituxan is an anti-CD20 antibody which preferentially depletes from blood B-cells, thus it is an ideal agent for "*in* *vivo*" *purging*. Due to the potential for synergy with chemotherapy it may enhance the effectiveness of the salvage regimen and due to its long half life it may offer a therapeutic benefit lasting through the high dose *treatment*. We enrolled thirty patients in a protocol employing a common mitoxantrone ifosfamide-etoposide salvage regimen (MINE) with rituxan for salvage and mobilization of stem cells...

...chemotherapy to achieve cytoreduction; stem cells were collected with the administration of 10 mcg/kg of GCSF or 500 mcg GMCSF after the last MINE *treatment*. *Rituximab* was administered at the dose of 400 mg/2 on day-7, 1 and 8 in relation to the last MINE administration. Stem cell collection...

...bcl-2 translocation or clonal immunoglobulin gene rearrangement (nested PCR sensitiveity 1:100,000) was negative in 10 patients and positive in 5. No unusual *transplant* complications were noted. With a median follow up after SCT of 15 months, 4 patients progressed (of which 3 succumbed) while another patient died from *transplant*-related complications. Molecular status of the stem cells did not predict long term outcome. However repeated blood PCR at 3 months after the procedure in...
DESCRIPTORS:
...DISEASES: blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*

4/3,K/13 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13591644 BIOSIS NO.: 200200220465
Autologous stem cell transplants combined with Rituximab for relapsed follicular lymphoma achieve prolonged clinical and molecular remissions.
AUTHOR: Buckstein Rena J(a); Imrie Kevin R(a); Spaner David(a); Mangel Joy (a); Tompkins Kirsty(a); Crump Michael; Coovadia Ahmed(a); Reis Marciano (a); Romans Robert(a); Pennell Nancy(a); Robinson Jean B(a); Hewitt Karen (a); Richardson Pat(a); Lima Ana(a); Pavlin Peggy(a); Boudreau Angela(a); Gitelson Elena(a); Berinstein Neil L(a)
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JOURNAL: Blood 98 (11 Part 1):p680a November 16, 2001
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CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Introduction: The benefits of high dose *therapy* in follicular lymphoma are controversial. To maximize response rates and remission durations, we have transplanted patients with relapsed, higher-risk, chemosensitive follicular lymphoma (REAL 1-2) and consolidated with *Rituximab* 375 mg/m2X4 infusions at 2 and 6 months post *transplant* (8 infusions total). The patients also received '*in*-*vivo*' *purging* with a single dose of *Rituximab* 3-5 days prior to stem cell collection. All patients must have achieved 75% reduction tumor bulk and <15% bone marrow positivity to undergo *transplant*. De-bulking chemotherapy was primarily either CHOP (n=9) and/or DHAP (n=14) with a median of 4 cycles given. Conditioning chemotherapy was CBV. Results: Since September 1998, 21 patients have been transplanted in this fashion. No peri-*transplant* mortality occurred. Patients engrafted and became plt transfusion independent at a median of 10 days. No late engraftment failures occurred. With a median follow-up of 23.8 mos overall (range 1.8-33 mos), 1 patient has relapsed at 21 mos post *transplant*, 1 patient has died at 7.2 mos of presumed septic causes. The remainder remain in either CR (n=4) or nCR (n=16). The...

...grade 4), pulmonary aspergillosis (n=2 grade 3), and elevated creatinine (n=1, grade 3). Although grade 2-3 neutropenia was frequently observed during first *Rituximab* infusions post *transplant*, patients were largely asymptomatic. Serial molecular responses by nested PCR of bcl-2 gene rearrangement or V(D)J clonality in PB/BM samples have been obtained in 12/21 of patients. 10/11 stem cell grafts were PCR positive, despite *Rituximab* purging. 9/12 patients became PCR negative at 2 months post *transplant* (pre *Rituximab* course 1) and the 3 patients still positive at this point (2 weakly) all achieved PCR negativity by 6-9 months. 90% of patients were PCR- at 6 months, prior to *Rituximab* course 2. PCR

negativity extends to months post *transplant*. Only one patient has become PCR positive in PB and BM at 24 months, but continues to remain in clinical remission. Conclusions: *Rituximab* immunotherapy as consolidation post high dose *therapy* and stem cell *transplant* for patients with relapsed follicular lymphoma is associated with high rates of durable clinical and molecular remissions. A single infusion of *Rituximab* prior to stem cell harvesting may be insufficient for '*in* *vivo*' *purging* although the clinical significance of *graft* positivity by molecular methods remains unknown. Strategies to eliminate molecular evidence of disease in the stem cell grafts and to combine *Rituximab* with other immunomodulators (ie Interferon) are currently being explored.

DESCRIPTORS:
...DISEASES: blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*

4/3,K/14 (Item 3 from file: 5)

13591630 BIOSIS NO.: 200200220451

Rituximab during autologous stem cell transplantion for lymphoma produces lymphoma free grafts in most patients by PCR and clonogenic assays.

AUTHOR: Flinn Ian W(a); Jones Richard J(a); Goodrich Amy(a); Carter-Brookins Denise(a); Moss Thomas J; Loper Kathy(a); Noga Stephen J (a); Berdeja Jesus G(a); Ambinder Richard F(a)
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ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The efficacy of autologous stem cell *transplantation* for patients with lymphoma is complicated by residual disease remaining in the patient despite the high dose *therapy* and the re-introduction of neoplastic cells with the auto *graft*. We are conducting a trial of *rituximab* used during stem cell mobilization and as a post *transplant* adjuvant in an attempt to overcome both of these obstacles. Tumor contamination of the PBSC *graft* is being measured with lymphoma colony formation and with PCR. Patients with NHL received 375 mg/m2 of *rituximab* day 1 of mobilization, followed by cyclophosphamide 2.5 gm/m2 day 4, GM-CSF 10 ug/kg days 1-7 and G-CSF 10...

...CD 34/kg are collected. The preparative regimen consisted of either cyclophosphamide and total body irradiation or busulfan and cyclophosphamide. GM-CSF is used post-*transplant*. Four weekly doses of *rituximab* are given post-*transplant* 7 days after plts reach 20,000/mm3. Sixty-five patients (45M:20F), median age 52 (range 31-65) have started *therapy*. Diagnoses include 36 follicular center cell, 10 mantle cell, 13 SLL/CLL, 4 marginal zone and 2 Waldenstrom's. Patients had receive a median of 2 (range 1-4) prior therapies. Sixteen patients were in complete remission, 43 in partial remission and 6 in early relapse at time of *transplant*. Fifty-seven of 65 patients were successfully mobilized (median 14.1X106 CD 34/kg, range 2.24X106-60.8X106 CD 34/kg). Fifty-one patients...

...the 57 patients. The number of stem cell grafts free of lymphoma contamination before and after CD34 selection is given. The 4 weekly doses of *rituximab* were generally well tolerated as was, the *therapy* in general. However, several significant unusual late adverse events have been, noted in the day 60 to one year post-*transplant* period including

3 deaths (1 @ day 125 f viral hepatitis, 1 @ day 190 [redacted]m aspergillosis, and 1 @ day 325 from pseudomonas sepsis), neutropenia, disseminated and...

...infection. With a median follow-up of 195 days, the event-free survival is 82.8% at both 1 and 2 years. We conclude that *in* *vivo* *purging* with *rituximab* and CD34 selection may produce a lymphoma free *graft* in many patients. Further follow-up is required to evaluate a potential for increased late infectious complications.

4/3,K/15 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13528606 BIOSIS NO.: 200200157427
A sequence of immuno-chemotherapy with Rituximab, mobilization of in vivo purged stem cells, high-dose chemotherapy and autotransplant is an effective and nontoxic *treatment* for advanced follicular and mantle cell lymphoma.
AUTHOR: Lazzarino Mario(a); Arcaini Luca(a); Bernasconi Paolo(a); Alessandrino Emilio P(a); Gargantini Livio; Cairoli Roberto; Orlandi Ester(a); Astori Cesare(a); Brusamolino Ercole(a); Pagnucco Guido(a); Colombo Anna A(a); Calatroni Silvia(a); Iacona Isabella; Regazzi Mario B; Morra Enrica
AUTHOR ADDRESS: (a)Division of Hematology, University of Pavia, IRCCS Policlinico San Matteo, Pavia**Italy
JOURNAL: Blood 98 (11 Part 2):p394b November 16, 2001
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ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

A sequence of immuno-chemotherapy with Rituximab, mobilization of in vivo purged stem cells, high-dose chemotherapy and autotransplant is an effective and nontoxic *treatment* for advanced follicular and mantle cell lymphoma.

ABSTRACT: Options for relapsed/refractory indolent lymphoma include chemotherapy, immunotherapy, and high-dose *therapy* with autologous progenitor cells support. The best combination of these approaches, however, is not defined. We developed a *treatment* program that combines chemotherapy, immunotherapy, high-dose *therapy* and autotransplant in a sequence of 4 phases, each designed to play a specific role in tumor eradication. This program was applied to 10 patients...

...bcl-2 or bcl-1 rearrangement in blood and marrow achieved a molecular response. Phase 2, immuno-chemotherapy, consisted of two six-day courses with *Rituximab* 375 mg/m2 on day 1, vincristine 2 mg on day 2, and cyclophosphamide 400 mg/m2 from day 2 to day 6. After this...

...bcl-2 or bcl-1 rearrangement showed disappearance of the signal from blood and marrow. The combination was well tolerated with negligible toxicities. Phase 3, *in* *vivo* *purging* and stem cells mobilization, coupled *Rituximab* 375 mg/m2 on day 1 and day 9 with cytarabine 2 g/m2/12h on day 2 and day 3, plus G-CSF from...
...combination was effective in mobilizing an adequate number of progenitor cells that were PCR-negative in all informative cases. Phase 4 consisted of high-dose *therapy* with BEAM followed by rescue with autologous progenitor cells and two doses of *Rituximab* 375 mg/m2 on day 14 and day 21 after *transplant*. Autograft was performed in nine patients. One patient with mantle cell lymphoma progressed pre-*transplant*. The hematopoietic recovery was regular in all cases. The median time to neutrophils over 500 was 12 days, and to platelets over 20,000 was 8

days. After a median follow-up of 10 months (3-15) after transplant*, all patients are in clinical complete remission. The six patients with molecular marker of disease had persistently negative PCR for bcl-2 or bcl-1 rearrangements in blood and marrow. This sequence of chemotherapy, immuno-chemotherapy, stem cell mobilization with *in* *vivo* *purging*, and autotransplant, organized in 4 blocks of *treatment*, was simple to administer and devoid of toxic effects. It permits rapid attainment of clinical and molecular response and enables the harvest of lymphoma-free ...

DESCRIPTORS:
...DISEASES: blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*

4/3,K/16 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13524421 BIOSIS NO.: 200200153242
Reduced-intensity *rituximab*-BEAM-CAMPATH allogeneic *transplantation* for indolent non-Hodgkin's lymphoma.
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JOURNAL: Blood 98 (11 Part 1):p188a November 16, 2001
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RECORD TYPE: Abstract
LANGUAGE: English

Reduced-intensity *rituximab*-BEAM-CAMPATH allogeneic *transplantation* for indolent non-Hodgkin's lymphoma.

ABSTRACT: Indolent non-Hodgkin's lymphomas are theoretically curable through allogeneic haematopoietic stem cell *transplantation* (HSCT). The applicability of allogeneic HSCT is however restricted by advanced age, coexisting morbidity and toxicity of standard conditioning regimens. Recently, reduced intensity regimens have significantly reduced early morbidity and mortality and extended the availability of allogeneic HSCT and potential benefits of *graft*-versus-lymphoma (GvL) effects to patients hitherto ineligible. We examine the efficacy of BEAM-CAMPATH (BCNU 300mg/m2 day -6; Cytarabine 200mg/m2 bd days...

...Melphalan 140mg/m2 day -1; CAMPATH-1H 20mg days -5 to -1) as conditioning for allogeneic HSCT in indolent CD20 positive non-Hodgkin's lymphomas. *Rituximab* delivered within 120 days pre-conditioning was used as *in*-*vivo* *purging*. Minimal residual disease was assessed by polymerase chain reaction (pcr) for bcl-2/IgH translocations, and chimerism by X,Y-FISH or pcr amplification of...

...composite follicular-mantle cell lymphoma) with advanced stage (5 Ann Arbour stage IVB, 1 stage IIIA) disease have thus far been recruited (1 without pre-*transplant* *rituximab*). The median age at diagnosis was 48.2 (34.0-52.7) years and at *transplant* 50.9 (34.2-55.8) years. At *transplant*, all were in partial remission after a median of 3 previous courses of chemotherapy (2-7). All initial stage IV patients had continued marrow infiltration...
...of 4.76X106/kg (2.9X106-6.95X106) and 1 bone marrow from a volunteer-unrelated donor with 3.45X106/kg CD34+ cells. Immediate post-*transplant* morbidity was limited to NCIC grade 1-2 stomatitis;

nausea/vomiting, and grade 3 febrile neutropenia. Neutrophil (>0.5X109/1) and platelet (>20X109/1) regeneration occurred at medians of 12.5 (11-29) and 12.0 (10-50) days respectively. Grade II skin and liver *graft* -versus-host disease (GvHD) occurred in 1 patient and limited chronic GvHD in another (D+129). All were alive at a median follow-up of 190.5 (105-385) days with ECOG performance status 0-1. Clinical and radiological complete remission following *transplant* continued in 4 patients with 2 demonstrating very weak pcr positivity and 1 persistently negativity. Progressive disease occurred in 2 patients. Both were strongly pcr positive following *transplant*. One developed rapidly progressive nodal disease at D+80, the other radiological evidence of slowly progressive nodal disease at D+99. Both failed to respond nodally to post-*transplant* *rituximab* although the former became pcr negative and had morphological clearance of marrow. Donor lymphocyte infusion (DLI) resulted in regression of nodal disease and re-establishment of predominant donor chimerism. Although follow-up is short, reduced intensity allogeneic HSCT with BEAM-CAMPATH conditioning appears to be safe and potentially curative. A *graft* versus lymphoma effect is demonstrable. Further investigation is required into the role of *Rituximab* in this setting, and into any potential anti-lymphoma properties of CAMPATH. Improved sensitivity in quantitative MRD methodology may allow better accuracy in scheduling *rituximab* and/or DLI in the post-HSCT setting.

DESCRIPTORS:
...DISEASES: blood and lymphatic disease, immune system disease, neoplastic disease, pathology, *therapy*;

4/3,K/17 (Item 6 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

13524039 BIOSIS NO.: 200200152860

Unexpected toxicities of combined rituximab and GM-CSF in autologous transplants for CD20 positive lymphoma.

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ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In an effort to prolong disease-free survival in patients with CD20+ lymphomas, a protocol utilizing *rituximab* for *in* *vivo* *purging* and prolonged administration of GM-CSF for increasing dendritic cell differentiation was initiated. In this study, patients are mobilized with cyclophosphamide (5grams/m2) and etoposide (1gram/m2) followed by *rituximab* (375mg/m2) weeklyX4 and GM-CSF 250mg/m2 day until completion of stem cell collection. *Transplantation* conditioning consists of busulfan 0.8mg/kg IVX16 doses and cyclophosphamide 120mg/kg in two divided doses. *Rituximab* (375mg/m2) is administered for four weekly doses beginning on day 0 and GM-CSF is given at 250mg/m2 daily beginning day+1 until day+30 post-*transplant*. Primary endpoints of this study are the ability to mobilize an adequate number of stem cells (gtoreq2.0X106 CD34+ cells/kg recipient weight) and time...

...G-CSF (5 mug/kg) and the same conditioning (except for busulfan given orally, 1mg/kgX16 doses) with G-CSF given until granulocyte recovery. No *rituximab* was included in the *therapy* of these previously treated patients. To date, ten patients have been treated on this study. For the entire group, two failed to mobilize and times...

...12 days. The 80% mobilization rate and times to engraftment of granulocytes and platelets matched our prior experience for patients with lymphoma who underwent autologous *transplant*. Although the primary endpoints showed no deleterious effects of this new *treatment*, the first four patients treated on this study had unexpected toxicities with late cytopenias and a high incidence of infections: Patient 1 had engraftment of...

...an episode of gram positive bacteremia. With resolution of her infection, her platelet count rose to normal. Patient 3 recovered his platelet count early post-*transplant* but developed gram-negative sepsis with profound thrombocytopenia; his platelet count then gradually rose to normal as his infection resolved. Patient 4 engrafted normally but...

...161. Because of the unexpected toxicities encounted by these first four patients the protocol was amended. The next 6 patients enrolled received no ritaximab post-*transplant* and GM-CSF was administered only until the ANC increased to gtoreq500/mm3 for 2 consecutive days post-*transplant*. Of the six patients treated on the revised protocol, two failed to mobilize, four went on to *transplant*. Only one of the four patients who underwent *transplantation* had late unexplained transient pancytopenia without clinical sequelae, and none had infections. Thus, the excess toxicity seen in the first four patients is attributable to the post-*transplant* *rituximab* and prolonged GM-CSF *therapy*. Additional studies on the effects of combined *rituximab*/GM-CSF *therapy* on molecular purging and dendritic cell number and function are underway.

4/3,K/18 (Item 7 from file: 5)

13523806 BIOSIS NO.: 200200152627

Effectiveness of Mabthera in advanced stages B-CLL and for *in* *vivo* *purging* autologous peripheral stem cell transplantation.

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ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

Effectiveness of Mabthera in advanced stages B-CLL and for *in* *vivo* *purging* autologous peripheral stem cell transplantation.

ABSTRACT: Mabthera (*Rituximab*, Roche) a chimeric monoclonal antibody directed against CD20 molecule, has been found effective in *treatment* of low grade lymphoma. The use of Mabthera in CLL is still controversial because of low expression of CD20 antigen on CLL cell comparing to...

...and 2 with de novo PLL. All but 2 were heavily previously treated, 4 of them relapsing after APSCT. Mabthera was given either as salvage *therapy* in 6 patients who were refractory to chemotherapy, or to eradicate minimal residual disease (MRD) in chemosensitive patients before harvesting of PSC (7 patients). Four...

...after Mabthera administration. In the second group of chemoresponsive patients treated with Mabthera, 6 entered in complete remission and one in good PR allowing an *in* *vivo* *purging* of the harvest. Three were autografted and retreated with Mabthera post-*transplant*, two remained in CR for 6 and 15 months, one developed a mild B cell clone 12 months

after *transplant*. In clusion, Mabthera is effective in chemosensitive CLL improving the quality of response and allowing *in* *vivo* *purging* before stem cell harvesting. Two PLL patients responded to combination of chemotherapy and Mabthera and achieved CR.
DESCRIPTORS:
...DISEASES: blood and lymphatic disease, drug *therapy*, immune system disease, neoplastic disease, surgery

4/3,K/19 (Item 8 from file: 5)

13501181 BIOSIS NO.: 200200130002
Molecular response to anti Cd20 (Rituximab) *therapy* in relapsed follicular lymphoma.
AUTHOR: Giraldo Pilar(a); Pelegrin Fatima; Palomera Luis(a); Recasens Valle (a); Najera Maria J(a); Perdiguer Luis(a); Puente Fernando(a); Rubio-Felix Daniel(a)
AUTHOR ADDRESS: (a)Hematology, SAHH Cooperative Study Group, Zaragoza** Spain
JOURNAL: Blood 98 (11 Part 1):p135a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

Molecular response to anti Cd20 (Rituximab) *therapy* in relapsed follicular lymphoma.

...ABSTRACT: gene translocation is related with frequent relapses. Purpose: To determine the efficacy of a Fludarabine-Mitoxantrone regimen (FLD/MTX) combined with monoclonal anti CD20 antibody (*Rituximab*) to induce clinical and molecular response in patients with relapsed follicular lymphoma (FL). Patients and methods: A prospective trial was conduced in 30 consecutive patients...

...Therapeutic schedule: FLD 30 mg/m2 days 1 to 3 and MTX 10 mg/m2 day 1, were administered monthtly for 4 months followed by *Rituximab* (375 mg/m2/weekly X4). Inclusion criteria: relapsed FL nodal biopsy with Bcl-2 immunohistochemistry expression, ECOG<3, normal liver and renal function, no concomitant diseases. Both clinical and molecular response were evaluated: PCR-ELISA assay for t(14;18) in peripheral blood (PB) and bone marrow (BM), prior to *therapy*, after FLD-MTX and two months after *Rituximab* *treatment* was completed. Results: mean age: 56.00+-12.44 (range 32-77); M/F: 12/18. ECOG: 0(22), 1(5), 2(2), 3(1...

...Response: 20 cases (66.6%) were valuable for response after FLD-MTX, showing 16 (80.0%) complete (CR-7) or partial response (PR-9). After *Rituximab* *therapy* (16 patients) the response rates were: CR-9 (56.3%) or PR-5 (31.2%) and 2 failures (12.5%), in 7 patients with CR an autologous stem cell *transplant* were performed. Molecular response: from 22 cases with positive BM t(14;18), 14 (63.6%) achieved molecular response, one after FLD-MTX. The median RFS of the group is 23 months. After 24 months of follow-up 79% are alive. Comments: FLD-MTX *therapy* induces clinical response in 80% of relapsed FL patients, with CR rates of 35.0%. *Rituximab* *therapy* does not influence but improves CR rates (56.3%). Furthermore it is capable to obtain *in* *vivo* *purging* in 77.2% of cases. In our opinion combined FLD-MTX chemotherapy plus *Rituximab* could be a good therapeutic scheme previously to stem-cell harvesting.
DESCRIPTORS:
...DISEASES: blood and lymphatic disease, drug *therapy*, immune system disease, neoplastic disease

4/3,K/20 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13112979 BIOSIS NO.: 200100320128
Relapsed follicular lymphoma. Response to fludarabine-mitoxantrone regimen and monoclonal anti CD20 (Rituximab).
AUTHOR: Giraldo Pilar(a); Pelegrin Fatima(a); Palomera Luis(a); Recasens Valle(a); Najera Maria J(a); Puente Fernando(a); Perdiguer Luis(a); Rubio-Felix Daniel(a)
AUTHOR ADDRESS: (a)SAHH, Zaragoza**Spain
JOURNAL: Blood 96 (11 Part 1):p730a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Purpose: To determine the efficacy of a Fludarabine/Mitoxantrone regimen (FLD/MTX) combined with monoclonal anti CD20 antibody (*Rituximab*) to induce clinical and molecular remissions in patients with relapsed Follicular lymphoma(FL). Patients and methods: A prospective trial was conduced in 18 consecutive relapsed...

...Therapeutic schedule: FLD: 30 mg/m2/days 1 to 3 and MTX 10 mg/m2/day 1, were administered monthly for 4 months followed by *Rituximab* (375 mg/m2/weekly X4). Inclusion criteria: relapsed nodal follicular NHL with Bcl-2 and CD20 positive expression, ECOG<3, normal liver and renal function, no concomitant diseases. Both clinical and molecular responses were evaluated; PCR assays for the t(14;18) in peripheral blood and bone marrow, prior to *therapy*, after FLD-MTX chemotherapy and after *Rituximab* *treatment* was completed. Results: 13 males and 5 females, mean age 52.3+-13.4(range: 32-77), ECOG: 0 (11), 1 (3), 2 (2), 3 (2). Clinical stage II (4), III (5), IV (9). No of previous therapies 1 (10), 2 (3) and 3 or more (5). Previous to *therapy*, bone marrow showed positive PCR t(14;18) in 10 cases (55.5%), and 4 (22.22%) were positive in peripheral blood. Response: 16 patients were evaluate for response, after FLD-MTX *therapy*, 5 patients showed CR (31.25%), 10 PR (62.50%) and 1 F (6.25%). After *Rituximab* *therapy* (15 patients) the response rates were: CR 9 (60.0%), PR 5 (33.33%) and F 1 (6.66%). Molecular response: according to 10 cases with positive PCR t(14;18) in bone marrow, 8 (80.0%) achieved molecular remission, one after FLD/MTX *therapy*, and was excluded for *Rituximab* *therapy*- 1 patient is continuously PCR t(14;18) positive and the remaining is under *therapy*. Comments: FLD-MTX *therapy* induces clinical response in 93.75% of patients with relapsed FL, with a CR rates of 31.25%. *Rituximab* *therapy* does not influence overall response but improves CR rates (60.0%). Furthermore it is capable to obtain *in* *vivo* *purging* in 77.77% of cases. For these reasons combined FLD/MTX chemotherapy plus *Rituximab* could be a good therapeutic scheme to produce *in* *vivo* *purging* previously to stem-cell harvesting, in patients undergoing autologous stem-cell *transplantation*.

4/3,K/21 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13110425 BIOSIS NO.: 200100317574
Immune reconstitution after autologous CD34-positive selected peripheral blood stem cell *transplantation* (PBSCT) combined with *Rituximab* for

refractory B-cell non-Hodgkin's lymphoma.
AUTHOR: Flohr Thomas(a); Hess Georg R(a); Kreiter Sebastian(a); Meyer Ralf G(a); Huber Christoph(a); Derigs Guenter(a)
AUTHOR ADDRESS: (a)IIIrd Med. Department, Johannes Gutenberg-University, Mainz**Germany
JOURNAL: Blood 96 (11 Part 1):p384a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

Immune reconstitution after autologous CD34-positive selected peripheral blood stem cell *transplantation* (PBSCT) combined with *Rituximab* for refractory B-cell non-Hodgkin's lymphoma.

ABSTRACT: Combining ex vivo CD34 positive selection and use of *Rituximab* for *in* *vivo* *purging* leads to effective tumor cell depletion in autologous grafts of pts with B-NHL. This strategy involves the risk of prolonged immunodeficiency post *transplantation* by intensive B- and T-cell depletion. For this reason we intensively studied lymphoid reconstitution in this setting with special regard to CMV serostatus and occurrence of CMV reactivation post PBSCT. Pts with relapsed or refractory CD20+ B-NHL received *Rituximab* combined with DexaBEAM for stem cell mobilization. Stem cell products were purged using the Clinimacs device. Two doses of *Rituximab* were administered as part of conditioning. Reconstitution of lymphocyte subsets were characterized by flowcytometric analysis using antibodies for CD19, CD20, CD3, CD2, CD16/56, CD4...

...cell-subpopulation explicites an activated phenotype coexpressing the markers CD38, CD57, HLADR. The present study confirms the severe combined immunodeficiency status of pts post autologous *transplantation* of CD34 selected peripheral blood stem cells. The lymphoproliferation seen in pts under CMV infection remarkebly alters the composition of the cellular immune system and...
DESCRIPTORS:
...DISEASES: blood and lymphatic disease, immune system disease, neoplastic disease, refractory, *treatment*;

4/3,K/22 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13110044 BIOSIS NO.: 200100317193
Primary autologous stem cell transplantation in mantle cell lymphoma: Clinical and molecular response.
AUTHOR: Geisler Christian H(a); Elonen Erkki; Johnson Anna; Kolstad Arne; Andersen N S(a)
AUTHOR ADDRESS: (a)Hematology, Rigshospitalet, Copenhagen**Denmark
JOURNAL: Blood 96 (11 Part 1):p794a-795a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

...ABSTRACT: mg/m2, cyclophosphamide 1200 mg/m2, vincristine 2 mg, prednisolone 100 mg) were offered high-dose chemotherapy with BEAM or

BEAC and autologous ste[redacted]cell *transplantation* with per[redacted]heral-blood stem cells. Stem cells were harvested following a 4th series of maxi-CHOP + filgrastim. Purging was optional. At diagnosis a molecular tumour...
...5-40). Twenty-eight have responded to maxi-CHOP (9 CR and 19 PR) whereas 9 have failed. Of the 28 responders 25 have reached *transplantation*. Posttransplant, 22 achieved or maintained CR, 2 PR and 1 progressed. Subsequently 2 have relapsed and one died of unrelated cause. Survival: On intent-to...

...for molecular response, 6 were PCR-negative. Of these one has relapsed. Stem-cell Purging: Methods used were mainly CD34+ cell selection (12 pts) or *in*-*vivo* *purging* with *Rituximab* 375 mg/m2 single infusion (4 pts). By a quantitative RT-PCR against the available clonal marker, the mean absolute No.s of tumor cells (TC) X 106 given back to the patients at *transplant* were as follows: In 7 unpurged cases 37 (range 3-60), in 12 CD34+ cell selected cases 1.7 (3-60) and in 4 in-vivo purged cases 13.3 (5-30). Conclusions: Primary *treatment* with high-dose *therapy* and autologous stem cell *transplantation* in MCL is promising, but a significant proportion fails *treatment* before reaching *transplant*. Molecular remission is possible, but the clinical significance is not yet known. A significant No. of tumor cells are given back, which can be reduced one log by CD34+ cell selection. A revised Nordic MCL protocol with intensified induction *treatment* and purging efforts is now being activated.

4/3,K/23 (Item 12 from file: 5)

13086695 BIOSIS NO.: 200100293844
Efficiency of *in* *vivo* *purging* with *rituximab* followed by high-dose *therapy* (HDT) with autologous peripheral blood stem cell *transplantation* (PBSCT) in B-cell non- Hodgkin's lymphomas (NHL). A single institution study.
AUTHOR: Haioun C(a); Delfau-Larue M H(a); Beaujean F(a); Beaumont J L(a); Belhadj K(a); Pautas C(a); Kirova Y(a); Allain A(a); Gaulard P(a); Farcet J P(a); Reyes F(a)
AUTHOR ADDRESS: (a)CHU Henri Mondor, Creteil**France
JOURNAL: Blood 96 (11 Part 1):p184a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

Efficiency of *in* *vivo* *purging* with *rituximab* followed by high-dose *therapy* (HDT) with autologous peripheral blood stem cell *transplantation* (PBSCT) in B-cell non- Hodgkin's lymphomas (NHL). A single institution study.

ABSTRACT: HDT with PBSCT is a *treatment* option for patients (pts) with advanced follicular, marginal and mantle cell lymphoma. In this setting, frequent contamination of PBSC harvests by tumor cells may contribute to relapse. Anti-CD20 monoclonal antibody (*Rituximab*) induce clinical response in such lymphomas (McLaughlin JCO 16:2825, 1998; Foran JCO 18:317, 2000) and is efficient in removing circulating B-cell from the peripheral blood (PB). We therefore hypothezized that *Rituximab* may be an useful *in* *vivo* *purging* agent prior to *transplant* *therapy*. From 05/98 to 05/00, 12 pts with relapsed follicular lymphoma (n = 9), transformed marginal zone (n = 2) and mantle cell (n = 1) lymphomas with bone marrow involvement and PCR-detectable molecular marker were treated with 4 courses of 375mg/m2 each of *Rituximab*. At the time of

treatment, pts with f icular lymphoma had receive no ior chemotherapy for their relapse and the other 3 pts were considered in 1st partial response (PR) after an anthracyclin-containing regimen. All the pts were in PR after *Rituximab*. With a median delay of 2 months after the last infusion of *Rituximab*, a mobilization regimen was delivered, consisting in Cyclophosphamide (Cy) 4,5g/m2 and VP16 450mg/m2 at d1 with G-CSF (5mug/kg) from d5...

...106 CD34 cells/kg harvested (3-21) and 1 leukapheresis (1-3). As of 08/00, 11 of the 12 patients (1 pt is on *therapy*) completed HDT with Cy (60mg/kg d-6 and d-5), VP16 (300mg/m2 d-6 to d-4) and a single dose total body irradiation at d-1 (8Gy). In all the pts, PCR analysis was performed in PB before *Rituximab* and in the leukapheresis product with bcl2-JH (n = 8), bcl1-JH (n = 1) or CDR II/III-specific primers (n = 3). At the present...

...9 out of 12 (75%). Engraftment to ANC gtoreq500 occurred at a median of 14 days similar to historical data for NHL not receiving pre-*transplant* *Rituximab*. With a median follow-up of 12 months, the 11 transplanted pts are alive, 10 in clinical complete remission (PCR leukapheresis product/PCR follow-up: -/- 6, +/+ 1) and one with progressive disease (-/+). We conclude that combination of *Rituximab* and HDT is effective to eliminate clinical tumor burden and minimal residual disease. A longer follow-up will be necessary to determine the molecular and...

...METHODS & EQUIPMENT: high-dose *therapy*--...

...*in* *vivo* *purging*--

4/3,K/24 (Item 13 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

12287410 BIOSIS NO.: 200000045277

***In* *vivo* *purging* with *rituximab* during stem cell *transplantation* for indolent lymphoma.**

AUTHOR: Flinn Ian W(a); O'Donnell Paul(a); Noga Stephen J(a); Moss Tom; Loper Kathy(a); Grillo-Lopez Antonio; Kunkel Lori; Vogelsang Georgia(a); Goodrich Amy(a); Abrams Ross(a); Lopategui Jean R; Jones Richard J(a); Ambinder Richard F(a)

AUTHOR ADDRESS: (a)Division of Hematologic Malignancies, Johns Hopkins Oncology Center, Baltimore, MD**USA

JOURNAL: Blood 94 (10 SUPPL. 1 PART 1):p638a Nov. 15, 1999

CONFERENCE/MEETING: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December 3-7, 1999

SPONSOR: The American Society of Hematology

ISSN: 0006-4971

RECORD TYPE: Citation

LANGUAGE: English

***In* *vivo* *purging* with *rituximab* during stem cell *transplantation* for indolent lymphoma.**

DESCRIPTORS:

...DISEASES: blood and lymphatic disease, immune system disease, neoplastic disease, *treatment*

?ds

Set	Items	Description
S1	508	(ANTI-CD20 OR ANTI-BP35 OR RITUXIMAB) (S) (GRAFT OR TRANSP-LANT OR TRANSPLANTATION)
S2	477	S1 AND (TREATMENT OR THERAPY)
S3	199	RD (unique items)
S4	24	S3 AND (IN (W) VIVO (W) PURGING)

?s s3 and ((graft (w) versus (w) host) or (host versus graft))

	199	S3
	271177	GRAFT
	406564	VERSUS

```
          724512  HOST
           27661  GRAFT(W)VERSUS(W)HOST
               0  HOST VERSUS GRAFT
      S5      18  S3 AND ((GRAFT (W) VERSUS (W) HOST) OR (HOST VERSUS
                  GRAFT))
?s s18 not s4
>>>"S18" does not exist
               0  S18
              24  S4
      S6       0  S18 NOT S4
?s s5 not s4
              18  S5
              24  S4
      S7      17  S5 NOT S4
?t s7/3,k/all
```

7/3,K/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

13745531 22276949 PMID: 12389620

Post-transplantation lymphoproliferative disease in Chinese: the Queen Mary Hospital experience in Hong Kong.

Au W Y; Lie A K W; Kwong Y L; Shek T W; Hawkins B R; Lai K N; Tang S C W; Lo C M; Fan S T; Liu C L; Chan G C F; Chau E M C; Chiu S W; Liang R

The University Department of Medicine, Queen Mary Hospital, University of Hong Kong, Peoples' Republic of China. auwing@hotmail.com

Leukemia & lymphoma (England) Jul 2002, 43 (7) p1403-7, ISSN 1042-8194 Journal Code: 9007422

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: In Process

Post-*transplantation* lymphoproliferative disease (PTLD) is an unique iatrogenic complication after bone marrow *transplantation* (BMT) and solid organ *transplantation* (SOTx). The pattern of EBV related lymphoma in Chinese is different from Caucasians. We surveyed the incidence, clinical and pathological spectrum of PTLD among 541 cases of allogeneic BMT, 145 cases of renal *transplant*, 35 cases of heart/lung *transplantation* and 146 cases of orthotopic liver *transplantation* (OLT). From 1994 to 2001, 13 consecutive cases of PTLD were diagnosed, ranging from disseminated NK cell lymphoma to localized plasmacytoma. Both donor and recipient...

...of PTLD at a median of 3 months. Complete and partial remission was only achieved in 3 and 2 cases, respectively, despite a range of *treatment* (reduced immuosuppression, explantation, radiotherapy, combination chemotherapy, donor lymphocytes, autologous marrow infusion and *rituximab*). Most responding patients died subsequently of rejection, infection and *graft* *versus* *host* disease (GVHD). The incidence of PTLD is not increased in Chinese patients. However, some patients may be at increased risk, especially mismatched allogeneic BMT, parental...

7/3,K/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

13532084 22197303 PMID: 12209356

Combination *treatment* of bullous pemphigoid with anti-CD20 and anti-CD25 antibodies in a patient with chronic *graft*-*versus*-*host* disease.

Szabolcs P; Reese M; Yancey K B; Hall R P; Kurtzberg J

Department of Pediatrics, Pediatric Stem Cell Transplant Program, Duke University Medical Center, Durham, NC, USA.

Bone marrow transplantation (England) Sep 2002, 30 (5) p327-9, ISSN 0268-3369 Journal Code: 8702459

Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

Combination *treatment* of bullous pemphigoid with anti-CD20 and anti-CD25 antibodies in a patient with chronic *graft*-*versus*-*host* disease.

In this case report we describe a novel *treatment* with two chimeric monoclonal antibodies (MoAb) targeting the autoimmune B cell clone responsible for bullous pemphigoid (BP) as a manifestation of steroid refractory chronic *graft*-*versus*-*host* disease (GVHD) that developed after unrelated cord blood *transplantation*. Monitoring the BP-specific circulating antibodies and CD25-expressing activated T lymphocyte subset led us to combine anti-CD20 (*Rituximab*) mediated B cell ablation with anti-CD25 (Daclizumab) *therapy* to block CD4(+) T cell help. Complete clinical and serologic response was achieved within 4 weeks of initiation of *therapy* allowing global immunosuppression to be dramatically reduced.

7/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13268057 21926815 PMID: 11929757

A humanized non-FcR-binding anti-CD3 antibody, visilizumab, for *treatment* of steroid-refractory acute *graft*-*versus*-*host* disease.

Carpenter Paul A; Appelbaum Frederick R; Corey Lawrence; Deeg H Joachim; Doney Kris; Gooley Theodore; Krueger James; Martin Paul; Pavlovic Sandra; Sanders Jean; Slattery John; Levitt Daniel; Storb Rainer; Woolfrey Ann; Anasetti Claudio

Division of Clinical Research, Fred Hutchinson Cancer Research Center, Seattle, USA. pcarpent@fhcrc.org

Blood (United States) Apr 15 2002, 99 (8) p2712-9, ISSN 0006-4971
Journal Code: 7603509

Contract/Grant No.: AI33484; AI; NIAID; AI40680; AI; NIAID; CA15704; CA; NCI; CA18029; CA; NCI; CA18221; CA; NCI; HL36444; HL; NHLBI

Document type: Clinical Trial; Journal Article; Multicenter Study
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

A humanized non-FcR-binding anti-CD3 antibody, visilizumab, for *treatment* of steroid-refractory acute *graft*-*versus*-*host* disease.

... and ability to induce apoptosis selectively in activated T cells. To test pharmacokinetics, safety, and immunosuppressive activity of visilizumab, 17 patients with glucocorticoid-refractory acute *graft*-*versus*-*host* disease (GVHD) were enrolled in a phase 1 study. Six patients were given 7 doses of visilizumab (0.25 or 1.0 mg/m(2...

...1 of 6 complete responses (CRs) and 5 partial responses (PRs), but all 6 patients died at a median of 87 days after starting visilizumab *therapy*. Single dosing resulted in 6 of 9 CRs, 3 PRs, and 7 of 11 patients surviving after 260 to 490 days (median, 359 days; P...

... of the first 7 patients. Based on rising EBV DNA titers, 5 of the next 10 patients were given the B cell-specific monoclonal antibody, *rituximab* . EBV DNA became undetectable and no overt PTLD developed. Visilizumab is well tolerated and has activity in advanced GVHD. A phase 2 study incorporating preemptive *therapy* for PTLD is warranted to determine the efficacy of visilizumab in GVHD.

Descriptors: Antibodies, Monoclonal--administration and dosage--AD; *Antigens, CD3--immunology--IM; *Graft vs Host Disease--drug *therapy*--DT

7/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12787257 21420170 PMID: 11529490

Low incidence of Epstein-Barr virus-associated posttransplantation lymphoproliferative disorders in 272 unrelated-donor umbilical cord blood transplant recipients.

Barker J N; Martin P L; Coad J E; DeFor T; Trigg M E; Kurtzberg J; Weisdorf D J; Wagner J

University of Minnesota Medical School, Minneapolis, USA. barke014@tc.umn.edu

Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation (United States) 2001, 7 (7) p395-9, ISSN 1083-8791 Journal Code: 9600628

Contract/Grant No.: NO1-HB-67139; HB; NHLBI; NO1-HB-67141; HB; NHLBI; PO1-CA65493; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Umbilical cord blood (UCB) is being increasingly used for *transplantation* , but the ability of neonatal T cells to regulate Epstein-Barr virus (EBV)-associated lymphoproliferation is unknown. Because UCB *transplantation* (UCBT) is associated with a relatively low infused dose of donor T cells, frequent donor-recipient HLA disparity, and use of antithymocyte globulin during conditioning...

...interval, 0.3%-3.7%) at 2 years. EBV-PTLD affected UCB recipients aged 1 to 49 years (median, 8 years), with 4 patients undergoing *transplantation* for leukemia and 1 for immunodeficiency. Patients received UCB grafts that were HLA matched (n = 1) or mismatched at 1 (n = 1) or 2 (n...

... loci. Diagnoses occurred at 4 to 14 months (median, 6 months) after UCBT, with 4 of 5 patients having preceding grade II to IV acute *graft*-*versus*-*host* disease and 1 being diagnosed at autopsy. *Treatment* of 4 patients consisted of withdrawal of immunosuppressive *treatment* and administration of *rituximab*, with 2 of 4 patients responding. Thus, the incidence of EBV-PTLD after unrelated-donor UCBT appears similar to that observed after *transplantation* using unrelated bone marrow (BM) and compares favorably with unrelated-donor T-cell-depleted BM *transplantation*. Because adoptive immunotherapy with donor lymphocytes is not an available option for recipients of unrelated-donor UCBT, new therapeutic strategies are needed, and *rituximab* appears promising.

...; Blood Donors; Child; Child, Preschool; Epstein-Barr Virus Infections --complications--CO; Fetal Blood; Herpesvirus 4, Human --growth and development--GD; Incidence; Infant; Lymphoproliferative Disorders--drug *therapy*--DT; Lymphoproliferative Disorders--etiology--ET; Middle Age; Retrospective Studies; Transplantation, Homologous--adverse effects--AE; *Treatment* Outcome; Virus Activation--drug effects--DE

7/3,K/5 (Item 5 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

12714584 21599727 PMID: 11739162

Nonablative allogeneic hematopoietic transplantation as adoptive immunotherapy for indolent lymphoma: low incidence of toxicity, acute *graft*-*versus*-*host* disease, and *treatment*-related mortality.

Khouri I F; Saliba R M; Giralt S A; Lee M S; Okoroji G J; Hagemeister F B ; Korbling M; Younes A; Ippoliti C; Gajewski J L; McLaughlin P; Anderlini P ; Donato M L; Cabanillas F F; Champlin R E

Department of Blood and Marrow Transplantation, University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, USA. ikhouri@notes.mdacc.tmc.edu

Blood (United States) Dec 15 2001, 98 (13) p3595-9, ISSN 0006-4971 Journal Code: 7603509

Document type: Clinical Trial; Journal Article

Languages: ENGLISH

Main Citation Owner: NL
Record type: Completed

Nonablative allogeneic hematopoietic transplantation as adoptive immunotherapy for indolent lymphoma: low incidence of toxicity, acute *graft*-*versus*-*host* disease, and *treatment*-related mortality.

This study investigated the use of a nonablative conditioning regimen to decrease toxicity and achieve engraftment of an allogeneic blood stem cell *transplant*, allowing a *graft* -versus-malignancy effect to occur. All patients had follicular or small cell lymphocytic lymphoma after relapse from a prior response to conventional chemotherapy. Patients received...

... days) and intravenous cyclophosphamide (1 g/m(2) given daily for 2 days or 750 mg/m(2) daily for 3 days). Nine patients received *rituximab* in addition to the chemotherapy. Tacrolimus and methotrexate were used for *graft*-*versus*-*host* disease (GVHD) prophylaxis. Twenty patients were studied; their median age was 51 years. Twelve were in complete remission (CR) at *transplantation* . All patients achieved engraftment of donor cells. The median number of days with severe neutropenia was 6. Only 2 patients required more than one platelet...

... being alive and in remission at 2 years was 84% (95% confidence interval, 57%-94%). Nonablative chemotherapy with fludarabine/cyclophosphamide followed by allogeneic stem cell *transplantation* is a promising *therapy* for indolent lymphoma with minimal toxicity and myelosuppression. Further studies are warranted to compare nonablative allogeneic hematopoietic *transplantation* with alternative *treatment* strategies.

Descriptors: Graft vs Host Disease--epidemiology--EP; *Hematopoietic Stem Cell Transplantation; *Immunotherapy, Adoptive; *Lymphoma, Small-Cell--*therapy*--TH; *Transplantation Conditioning--methods--MT; *Vidarabine--analogs and derivatives--AA...; Survival; Graft vs Host Disease--prevention and control--PC; Graft vs Tumor Effect; Immunosuppressive Agents--administration and dosage--AD; Lymphoma, Follicular--mortality--MO; Lymphoma, Follicular--*therapy*--TH; Lymphoma, Small-Cell--mortality--MO; Methotrexate--therapeutic use--TU; Middle Age; Platelet Transfusion; Recurrence; Remission Induction; Tacrolimus--therapeutic use--TU; Transplantation, Homologous; *Treatment* Outcome; Vidarabine--administration and dosage--AD

7/3,K/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10832352 20383460 PMID: 10929168

Anti-CD20 chimeric monoclonal antibody *treatment* of refractory immune-mediated thrombocytopenia in a patient with chronic *graft*-*versus*-*host* disease.

Ratanatharathorn V; Carson E; Reynolds C; Ayash L J; Levine J; Yanik G; Silver S M; Ferrara J L; Uberti J P

Blood and Marrow Stem Cell Transplant Program, Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor 48109, USA. vratanat@umich.edu

Annals of internal medicine (UNITED STATES) Aug 15 2000, 133 (4) p275-9, ISSN 0003-4819 Journal Code: 0372351

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Anti-CD20 chimeric monoclonal antibody *treatment* of refractory immune-mediated thrombocytopenia in a patient with chronic *graft*-*versus*-*host* disease.

BACKGROUND: Autoimmune thrombocytopenia in chronic *graft*-*versus*-*host* disease may represent an instance of B-cell dysregulation leading to clinical disease. OBJECTIVE: To attempt to treat refractory immune-mediated thrombocytopenia in a patient with chronic *graft*-*versus*-*host* disease

by using anti-CD20 chimeric monoclonal antibody. DESIGN: Case report. SETTING: Academic medical center. PATIENT: A patient with chronic *graft*-*versus*-*host* disease after allogeneic peripheral blood stem-cell *transplantation* who had severe refractory immune-mediated thrombocytopenia. INTERVENTION: Weekly infusion of *rituximab*, 375 mg/m2, for 4 weeks. MEASUREMENTS: Platelet count, CD3+ cell count, and CD19+ cell count. RESULTS: *Rituximab* *therapy* resulted in marked depletion of B cells in the peripheral blood and decreased levels of platelet-associated antibody. The increase in platelet count persisted despite tapering and discontinuation of immunosuppressive *therapy* for chronic *graft*-*versus*-*host* disease. CONCLUSION: The efficacy of *rituximab* for the *treatment* of immune-mediated thrombocytopenia suggests that this drug may have activity in other autoimmune diseases or chronic *graft*-*versus*-*host* disease.

Descriptors: Antibodies, Monoclonal--therapeutic use--TU; *Antigens, CD20 --immunology--IM; *Autoimmune Diseases--complications--CO; *Autoimmune Diseases--drug *therapy*--DT; *Graft vs Host Disease--complications--CO; *Thrombocytopenia--complications--CO; *Thrombocytopenia--drug *therapy* --DT

7/3,K/7 (Item 7 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10577181 20107430 PMID: 10642818

Use of *rituximab* and irradiated donor-derived lymphocytes to control Epstein-Barr virus-associated lymphoproliferation in patients undergoing related haplo-identical stem cell *transplantation*.

McGuirk J P; Seropian S; Howe G; Smith B; Stoddart L; Cooper D L

Blood and Marrow Transplant Program, Yale University School of Medicine, New Haven, Connecticut 06520-8032, USA.

Bone marrow transplantation (ENGLAND) Dec 1999, 24 (11) p1253-8, ISSN 0268-3369 Journal Code: 8702459

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Use of *rituximab* and irradiated donor-derived lymphocytes to control Epstein-Barr virus-associated lymphoproliferation in patients undergoing related haplo-identical stem cell *transplantation*.

Epstein-Barr virus-associated lymphoproliferative disorder (EBV-LPD) is an uncommon but potentially fatal complication of allogeneic stem cell *transplantation* . We report here two patients who underwent T cell-depleted mismatched-related stem cell *transplantation* for hematologic malignancies and required aggressive post-*transplant* immunosuppression for *graft*-*versus* *host* disease (GVHD). Both patients subsequently developed markedly elevated EBV-DNA titers in association with monoclonal, light chain-restricted B cell populations in the blood. Although immunosuppressive medications were rapidly tapered, neither patient could receive potentially curative *therapy* with unmanipulated donor-derived lymphocyte infusions (DLI) because of the substantial risk of severe GVHD. Therefore, both patients received repeated courses of *rituximab* , an anti-CD20 monoclonal antibody, in combination with irradiated DLI. This therapeutic strategy resulted in normalization of the elevated EBV-DNA titers and disappearance of the monoclonal B cell populations. Our results suggest that *rituximab* and possibly irradiated DLI played an important role in controlling early EBV-LPD in these two patients and may be an effective alternative therapeutic strategy for patients who develop EBV-LPD post *transplant* and are unable to receive unmanipulated DLI.

; Adult; Antigens, Viral--pharmacology--PD; Antineoplastic Agents --therapeutic use--TU; Blood Component Transfusion; Blood Donors; DNA, Viral--blood--BL; Graft vs Host Disease--drug *therapy*--DT; Hematologic Neoplasms--complications--CO; Hematologic Neoplasms--*therapy*--TH; Herpesvirus 4, Human--genetics--GE; Immunosuppression--adverse effects--AE;

Lymphocytes--immunology-[redacted]; Polymerase Chain Reaction

7/3,K/8 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13746899 BIOSIS NO.: 200200375720
Reduced-intensity *Rituximab*-BEAM-CAMPATH allogeneic haematopoietic stem cell *transplantation* (HSCT) for follicular lymphoma with quantitative monitoring of minimal residual disease.
AUTHOR: Ho A Y L(a); Devereux S(a); Mufti G J(a); Pagliuca A(a)
AUTHOR ADDRESS: (a)Department of Haematological Medicine, King's College Hospital, London**UK
JOURNAL: British Journal of Haematology 117 (Supplement 1):p37-38 May, 2002
MEDIUM: print
CONFERENCE/MEETING: British Society for Haematology 42nd Annual Scientific Meeting Brighton, UK April 15-18, 2002
ISSN: 0007-1048
RECORD TYPE: Citation
LANGUAGE: English

Reduced-intensity *Rituximab*-BEAM-CAMPATH allogeneic haematopoietic stem cell *transplantation* (HSCT) for follicular lymphoma with quantitative monitoring of minimal residual disease.
DESCRIPTORS:
DISEASES: cGVHD {chronic *graft* *versus* *host* disease...
...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*;
METHODS & EQUIPMENT: reduced intensity *rituximab*-BEAM-CAMPATH allogeneic hematopoietic stem cell *transplantation*--

7/3,K/9 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13621319 BIOSIS NO.: 200200250140
Prolonged failure free survival and molecular responses with nonablative allogeneic hematopoietic transplantation as adoptive immunotherapy for indolent lymphoma.
AUTHOR: Khouri Issa(a); Saliba Rima M(a); Giralt Sergio A(a); Lee Ming-Sheng; Okoroji Grace-Julia(a); Hagemeister Fredrick B; Korbling Martin(a); Younes Anas; Ippoliti Cindy(a); Gajewski James L(a); McLaughlin Peter; Anderlini Paolo(a); Donato Michele L(a); Cabanillas Fernando F; Champlin Richard E(a)
AUTHOR ADDRESS: (a)Department of Blood and Marrow Transplantation, Houston, TX**USA
JOURNAL: Blood 98 (11 Part 1):p744a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We investigated the use of a nonablative conditioning regimen to decrease toxicity and achieve engraftment of an allogeneic blood stem cell *transplant* (AST), allowing a *graft*-versus-malignancy effect to occur. We studied adult pts ageltoreq70 yrs who had follicular (N=18) or small lymphocytic lymphoma (N=2) after relapse from...

...3 days) and intravenous cyclophosphamide (C)(1 gm/m2 given daily for two days or 750 mg/m2 daily for 3 days. Nine pts received *rituximab* (R)375mg/m2X1 then 1g/m2 weeklyX3 in addition to the chemotherapy.

Tacrolimus (FK) and methotrexate was used for *graft*-*versus*-*host* disease (GVHD) prophylaxis. Twenty patients were studied. Median age was 51 years (range 31-68). Median prior chemoregimens was 2 (range 1-5). At the time of AST, 12 had responded to salvage *therapy* and were in gtoreq2nd CR, 6 in PR and 2 had PD. One had failed prior auto BMT. All pts acheived engraftment of donor cells...

...80% at 1 mo). The median number of days with severe neutropenia (<500 neutrophils) was six with no delay observed in the pts who received *rituximab*. Only 2 pts required more than 1 platelet transfusion. The median of RBC transfused was 1. The cumulative incidence of acute grade II-IV GVHD...

...85% (95% CI, 60% to 95%). Clonal cells were detected in 6 pts by PCR for bcl-2 pre-AST. All converted to PCR (-) post *transplant* as confirmed by 29 sequential samples. We conclude that nonablative chemotherapy with FCR followed by an AST is a promising *therapy* for indolent lymphoma with acceptable toxicity and myelosuppression.

DESCRIPTORS:
DISEASES: *graft*-*versus*-*host* disease {GVHD...
...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*

7/3,K/10 (Item 3 from file: 5)

13558086 BIOSIS NO.: 200200186907

In vivo model of novel CD20 suicide gene system.

AUTHOR: Introna Martino(a); Di Gaetano Nicola(a); Cittera Elena(a); Golay Josee(a)
AUTHOR ADDRESS: (a)Laboratory of Molecular Immunohematology, Istituto Mario Negri, Milano**Italy

JOURNAL: Blood 98 (11 Part 1):p421a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The use of the allogeneic bone marrow *transplantation* is hampered by the development of *graft* *versus* *host* disease (GVHD). Several attempts have been made to genetically manipulate T lymphocytes in order to control GVHD. We recently described a novel suicide gene system...

...on the transduction of T cells with human CD20 cDNA. CD20 gene modified T cells become susceptible to lysis following exposure to monoclonal anti-CD20 *Rituximab* antibody (Roche) and complement. Double positive CD3/CD20 T cells, in addition, can be rapidly selected by immunoaffinity columns and should not be immunogenic in...

...mantained this phenotype for over one year of continuous in vitro culture. Cells were completely lysed after three hours exposure to 5 mug/ml of *Rituximab* in presence of 25% human or mouse serum. We have then injected groups of C57/bl6 mice either i.p. or i.v with EL...

...that CD20 transduction did not alter tumour formation at various sites or survival by either route of administration. In order to test the efficiency of *Rituximab* administration in vivo, we chose the dose of

1X104 cell per mouse w h kills 100% of animals in 4-5 weeks. 150 mug *Rituximab* i.p., given either as a single dose at day +1 or as a repeated injection twice weekly for four weeks, protected 100% of the animals. We are presently evaluating quantitatively the efficacy of *Rituximab* *treatment* in vivo by amplifying the human CD20 molecule from different tissues of treated mice, using the Taqman technology. Our data demonstrate that CD20 modified T cells can be efficiently killed by *Rituximab* in vivo in this murine model. The mechanism of *Rituximab* induced killing will be further investigated.

7/3,K/11 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13558017 BIOSIS NO.: 200200186838
***Graft*-*versus*-*host* disease (GVHD) after non-myeloablative (NMA) versus myeloablative (MA) conditioning regimens in fully matched sibling donor hematopoietic stem cell transplants (HSCT): An update.**
AUTHOR: Couriel Daniel R(a); Khouri Issa F(a); Andersson Borje(a); Cohen Agueda(a); Saliba Rima(a); Delima Marcos(a); Martin Thomas(a); Giralt Sergio(a); Champlin Richard(a)
AUTHOR ADDRESS: (a)Blood and Marrow Transplant, UT MD Anderson Cancer Center, Houston, TX**USA
JOURNAL: Blood 98 (11 Part 1):p404a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

***Graft*-*versus*-*host* disease (GVHD) after non-myeloablative (NMA) versus myeloablative (MA) conditioning regimens in fully matched sibling donor hematopoietic stem cell transplants (HSCT): An update.**
...ABSTRACT: fludarabine ara-c and idarubicin (FLAG-IDA), n=25, cisplatin, fludarabine and ara-c (PFA), n=16, fludarabine and cyclophosphamide (FC), n=15 and FC-*rituximab* (FC-r), n=7. The MA group received IV busulfan and cyclophosphamide (IV BuCy) conditioning. All patients had 6/6 HLA-matched donors. GVHD prophylaxis...

...27), NHL (NMA 31, MA 1) and CLL (NMA 8). Most patients in the NMA group had advanced disease or comorbid conditions that prevented MA *treatment* . All but 7 patients in the NMA group and 17 in the MA group received peripheral blood stem cell (SC) transplants (92.5% and 63...

...GVHD was 45% and 40.4% (P=0.63, chi square test) in NMA patients (with documented engraftment) and in MA patients, respectively. To date, *transplant*-related mortality (TRM) was 20.2% (n=19) in patients receiving NMA transplants and 12.7% (n=6) in patients treated with MA BuCy (P...

...higher in the MA group. Severe aGVHD and chronic GVHD incidences were similar in both groups, despite differences age, diagnoses and SC source. GVHD and *transplant*-related mortality were similar in both groups. Despite differences in age and comorbidities, NMA transplants could be performed with a TRM comparable to MA conditioning...
DESCRIPTORS:
...DISEASES: blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, neoplastic disease, *therapy*; ...

...blood and lymphatic disease, immune system disease, neoplastic disease, *therapy*; *graft*-*versus*-*host* disease

7/3,K/12 (Item 5 from file: 5)

13524141 BIOSIS NO.: 200200152962
Graft-versus-lymphoma effect of donor leukocyte infusion in indolent lymphomas relapsed after T-cell depleted allogeneic stem cell transplantation, substantiated by real-time PCR quantitation and immunophenotyping.
AUTHOR: Mandigers Caroline(a); Verdonck Leo; Meijerink Jules; Schattenberg Anton(a); Tonnissen Evelyn; Raemaekers John(a)
AUTHOR ADDRESS: (a)Hematology, University Medical Center, Nijmegen** Netherlands
JOURNAL: Blood 98 (11 Part 2):p369b November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 2 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In case of relapsed hematologic disease after allogeneic stem cell *transplantation* (SCT) remission can still be induced by infusion of leukocytes derived from the original stem cell donor (DLI). Data on the effect of DLI in...
...and total body irradiation (n=4), or with additional idarubicin (n=3) stem cells from genetic identical sibling donors were infused. After SCT neither acute *graft*-*versus*-*host* disease (GVHD)gtoreqgrade 3 was seen, nor extensive chronic GVHD. The relapses were diagnosed at a median of 25 (range 12-73) months after SCT...

...of median 0.9 (range 0.1-1.0)X10*8 CD3+ cells per kg body weight. Three patients were treated with DLI as sole *therapy* and reached a complete remission; no acute GVHD and only limited chronic GVHD were seen in these patients. The other four patients received additional *therapy* before DLI. Three of them were treated with chemo- and/or radiotherapy, and one with anti-CD20 (*rituximab*). 3/4 Patients reached a partial remission and 1/4 a complete remission. In these four patients neither acute GVHDgtoreqgrade 3 was seen, nor extensive...

...the relapsed small lymphocytic lymphoma patients showed disappearance of the CD5+ CD19+ clone after DLI, corresponding with the clinically observed complete remission. DLI is effective *treatment* for relapsed indolent lymphoma after T-cell depleted SCT.
DESCRIPTORS:
DISEASES: *graft*-*versus*-*host* disease {GVHD...
...blood and lymphatic disease, drug *therapy*, genetics, immune system disease, neoplastic disease, surgery...

7/3,K/13 (Item 6 from file: 5)

13114839 BIOSIS NO.: 200100321988
Genetic modification of human T cells with CD20: A novel suicide system for the *treatment* of GVHD.
AUTHOR: Introna M(a); Casati C; Bambacioni F; Gaipa G; Golay J; Rambaldi A; Biondi A
AUTHOR ADDRESS: (a)Molecular Immunohematology Laboratory, Istituto Ricerche

Farmacologiche Mario N[redacted]i, Milano**Italy
JOURNAL: Blood 96 (11 Part 1):p214a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

Genetic modification of human T cells with CD20: A novel suicide system for the *treatment* of GVHD.

ABSTRACT: T lymphocytes are of paramount importance for the optimal *treatment* of bone marrow-transplanted patients. The possibility to genetically engineer T lymphocytes can contribute to improve their handling in a clinical setting. In particular, one...

...find strategies for rapid selection of transduced cells and, in addition, to render T lymphocytes susceptible to death in vivo (suicide gene) in case of *graft* *versus* *host* disease (GVHD). Finally the suicide gene should not immunogenic. We explored the possibility to introduce a single human gene that can at the same time...

...of purity (from 64% to 92% CD3/CD20 double positive cells in 7 different experiments). In vitro exposure to chimeric humanised monoclonal anti-CD20 antibody (*Rituximab*, Roche) in the presence of complement, results in effective (over 90%) and rapid (4 hours) killing of the transduced CD3/CD20 double positive human T...

...the parental cell line. The establishment of a murine T/CD20 in vivo model will now allow us to test the killing in vivo by *Rituximab* administration. This approach represents a new and alternative method of gene manipulation with a suicide gene for the production of drug responsive T cell populations...
DESCRIPTORS:
...DISEASES: immune system disease, *treatment*

7/3,K/14 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13112972 BIOSIS NO.: 200100320121
Humanized non-FCR-binding anti-CD3 antibody as *therapy* for glucocorticoid refractory acute GVHD.
AUTHOR: Carpenter P A(a); Corey L(a); Tso J Y; Anasetti C(a)
AUTHOR ADDRESS: (a)Clinical Division, Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA**USA
JOURNAL: Blood 96 (11 Part 1):p476a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

Humanized non-FCR-binding anti-CD3 antibody as *therapy* for glucocorticoid refractory acute GVHD.

...ABSTRACT: anti-CD3 mAb M291 led to HuM291, which retains murine CDRs but is a mutated human IgG2 with minimal FcR binding avidity (Cole et al, *Transplantation* 68:563, 1999). We have shown that HuM291 is much more

potent than OKT3 at causing apoptosis of activated T cells, while sparing resting T...

...I study of HuM291 in acute GVHD. Since June 1999, 12 patients with Grade III-IV acute GVHD, beginning 6-40 d (median 21) post-*transplant*, were refractory to 2 mg/kg MP plus CSP or FK506. In addition they received HuM291: 3 at 0.25 mg/m2 q.o.d...

...6/6 for >3 wks. Quantitative serial DNA PCR testing of plasma indicated reactivation of latent EBV in 8/12. 2/12 developed overt post-*transplant* lymphoproliferative disease. Two patients, whose EBV titer rose after HuM291, were treated with 1 dose of B cell-specific antibody, *Rituximab*. EBV became undetectable and PTLD did not occur. Manifestations of GVHD improved in all 12 patients. With 0.25 X 7 or 1.0 mg...

...for GVHD. Early Phase I testing of HuM291 indicates that mAb engineering can improve pharmacokinetics and abrogate dose-limiting cytokine release. EBV reactivation after HuM291 *therapy* is common in patients with advanced GVHD. The efficacy of preemptive *therapy* with *rituximab* will be tested in patients who demonstrate EBV replication based on serial monitoring of plasma DNA by quantitative PCR. Early efficacy data are encouraging. Accrual...
DESCRIPTORS:
DISEASES: acute GvHD {acute *graft*-*versus*-*host* disease...

7/3,K/15 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13112933 BIOSIS NO.: 200100320082
Prior *therapy* with anti-CD20 chimeric antibody (*Rituximab*) may decrease the risk of acute *graft*-*versus*-*host* disease (GVHD) in patients with non-Hodgkin's lymphoma receiving allogeneic stem cell *transplantation*.
AUTHOR: Ratanatharathorn Voravit(a); Bociek Robert G; Pavletic Steven Z; Lynch James C; Ferrara James L M(a); Uberti Joseph P(a)
AUTHOR ADDRESS: (a)Internal Medicine and Pediatrics, University of Michigan Medical Center, Ann Arbor, MI**USA
JOURNAL: Blood 96 (11 Part 1):p391a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

Prior *therapy* with anti-CD20 chimeric antibody (*Rituximab*) may decrease the risk of acute *graft*-*versus*-*host* disease (GVHD) in patients with non-Hodgkin's lymphoma receiving allogeneic stem cell *transplantation*.

ABSTRACT: Anti-CD20 chimeric antibody (*Rituximab*) is efficacious *treatment* for lymphoma expressing the CD20 antigen. B-cell depletion, resulting from *rituximab* *treatment*, may also potentially abrogate host B-cell antigen presentation to donor T cells, and thus diminish the risk of acute GVHD for patients undergoing allogeneic stem cell *transplantation* (alloSCT). To test this hypothesis, we retrospectively studied 37 consecutive patients with non-Hodgkin's lymphoma who received alloSCT between July 1998 and June 2000. Fourteen of these 37 patients received prior *rituximab* *therapy* for their lymphoma, and the remaining 23 patients were contemporaneous patients who did not receive *rituximab*. Patient's ages ranged from 23 to 66, with a median of 46. Patients receiving and not receiving *rituximab* were balanced with respect to numbers of prior chemotherapy regimen (P=0.09) and the

durations of disease p[illegible]or to *transplantation* (median 26 and 32 months, respectively (P=0.79). Peripheral blood stem cells (PSC) were used in 24 out of 28 related donor transplants. All...

...and the remaining 4 BM grafts were given to related-donor recipients. The sources of stem cells were 6BM and 17 PSC in the no-*rituximab* group, and 7 BM and 7 PBSC in the *rituximab* group (P=0.14). This study suggests the possible role host B-cell depletion in recipients of alloSCT as prophylaxis against acute GVDH. Animal models...

...the role of B-cell antigen presentation in the development of acute GVHD are being evaluated. Based on this preliminary observation, a prospective study of *rituximab* for the prevention of acute GVHD is planned.

7/3,K/16 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13104299 BIOSIS NO.: 200100311448
A dicistronic retroviral vector encoding HSV TK and CD20 for positive selection and conditional ablation of human T cells.
AUTHOR: Hu Jian-Da(a); Schmah Oliver(a); Finke Juergen(a); Veelken Hendrik (a)
AUTHOR ADDRESS: (a)Department of Hematology/Oncology, Freiburg University Medical Center, Freiburg**Germany
JOURNAL: Blood 96 (11 Part 2):p380b November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Donor lymphocyte infusions (DLI) are currently standard *treatment* for recurrent hematologic malignancy after allogeneic stem cell *transplantation*. A major limitation of DLI is the risk of inducing severe *graft*-*versus*-*host* disease (GvHD). Transduction of donor T cells with the "suicide gene" HSV thymidine kinase (TK) prior to DLI is an attractive approach to conditionally ablate GvHD-inducing donor T cells in vivo by systemic *treatment* with the prodrug gancyclovir (GCV). Genetic modification of primary T cells may be achieved with retroviral vectors, however, limited transduction efficiencies usually mandate a positive...

...reagents, (3) firm anchoring and lack of shedding due to four transmembrane domains, and (4) availability of a anti-CD20 antibody licensed for in vivo *therapy* (*rituximab*) which may be combined with GCV to enhance the efficacy of T cell elimination. Infectious LXTK20 supernatants were obtained by calcium phosphate transfection of Phoenix ...

...CD20 over a four week expansion period. As assessed by a metabolic XTT assay, growth of LXTK20-transduced, CD20-positive cells was completely inhibited by *treatment* with 1 mg/L GCV for 4 days. These data indicate that the retroviral vector LXTK20 facilitates efficient and rapid sorting of transduced cells and...
DESCRIPTORS:
DISEASES: *graft*-*versus*-*host* disease...

7/3,K/17 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13098780 BIOSIS NO.: 200100305929

Posttransplant lymphoproliferative disorder after non myeloablative stem cell transplantation.

AUTHOR: Arat Mutlu(a); Gurman Gunhan(a); Celebi Harika(a); Soydan Ender(a); Kuzu Ibynsu; Koc Haluk(a)
AUTHOR ADDRESS: (a)Hematology, Ankara University Medical School, Ibni Sina Hospital, Sihhiye, Ankara**Turkey

JOURNAL: Blood 96 (11 Part 2):p345b November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The interest for lowering the intensity of the conditioning regimen in the aim of lowering *transplant* related morbidity and mortality is still growing. Such regimens are expected produce less toxicity while allowing both engraftment and a mixed chimeric status, which can...

...ATG-Fludarabine-Ara-C) conditioning. Following the first DLI another DLI was performed preceding hematological and cytogenetical relapse. He received a 3rd DLI and interferon *therapy* (9MU/day s.c.) because of the persistent Ph+ positivity. After the completion of 1 year he was in complete hematological and cytogenetical remission and chimeric status was totally of donor origin. As extensive chronic *graft* *versus* *host* disease (cGVHD) developed, ATG was used for regression of mucosal and lichenoid lesions. In the 16th month of the *transplantation* the patient was readmitted to the hospital because of weight loss and testicular mass. On physical examination axillary lymph nodes were palpable. Hematological parameters were normal and serum biochemistry revealed elevated LDH levels. The immunosuppressive drugs were stopped and non-specific antiviral *therapy* was started. The testicular excisional biopsy and bone marrow trephine biopsy was reported as B- cell (CD20+, CD10+, CD43+) lymphoproliferative disorder. Though vigorous examination for EBV infection was negative, the patient was diagnosed as post *transplant* lymphoproliferative disorder and treated with COP. Because of the temporary regression of testicular lesion we treated the patient with CD20 monoclonal antibody (*rituximab*) and did not attempt to DLI because of extensive cGVHD. The patient did no respond to *rituximab* and died of progressive disease and underlying cGVHD in four months. Heavy immunosuppression (ATG, Fludarabine, CsA) used in NMA may have unexpected consequences. We described...

...course of a refractory PTLD, in a blastic phase CML patient, who achieved complete hematological and cytogenetical remission and complete donor chimeric status after allogeneic *transplantation* with NMA regimen and further DLIs.
METHODS & EQUIPMENT: antiviral *therapy*--...

...therapeutic method, transplantation *therapy*;

?ds

Set	Items	Description
S1	508	(ANTI-CD20 OR ANTI-BP35 OR RITUXIMAB) (S) (GRAFT OR TRANSP-LANT OR TRANSPLANTATION)
S2	477	S1 AND (TREATMENT OR THERAPY)
S3	199	RD (unique items)
S4	24	S3 AND (IN (W) VIVO (W) PURGING)
S5	18	S3 AND ((GRAFT (W) VERSUS (W) HOST) OR (HOST VERSUS GRAFT))
S6	0	S18 NOT S4
S7	17	S5 NOT S4

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?logoff
       23dec02 13:23:40 User259876 Session D448.2
            $5.51    1.722 DialUnits File155
               $3.78  18 Type(s) in Format  3
            $3.78  18 Types
     $9.29  Estimated cost File155
            $1.44    0.488 DialUnits File159
     $1.44  Estimated cost File159
           $14.43    2.576 DialUnits File5
              $40.25  23 Type(s) in Format  3
           $40.25  23 Types
    $54.68  Estimated cost File5
            $4.23    0.755 DialUnits File55
     $4.23  Estimated cost File55
            OneSearch, 4 files,  5.542 DialUnits FileOS
     $1.51  TELNET
    $71.15  Estimated cost this search
    $71.48  Estimated total session cost   5.626 DialUnits

### Status: Signed Off. (7 minutes)
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Status: Path 1 of [Dialog Information Services via Modem]

Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
******** HHHHHHHH SSSSSSSS?
Status: Signing onto Dialog
****
ENTER PASSWORD:
******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
Status: Connected

Dialog level 02.12.20D

Last logoff: 18dec02 13:13:49
Logon file001 23dec02 11:35:04
*** ANNOUNCEMENT ***
***
--File 515 D&B Dun's Electronic Business Directory is now online completely updated and redesigned. For details, see HELP NEWS 515.
***
--File 990 - NewsRoom now contains May 2002 to present records. File 993 - NewsRoom archive contains 2002 records from January 2002-April 2002. To search all 2002 records, BEGIN 990,993 or B NEWS2002.
***
--Alerts have been enhanced to allow a single Alert profile to be stored and run against multiple files. Duplicate removal is available across files and for up to 12 months. The Alert may be run according to the file's update frequency or according to a custom calendar-based schedule. There are no additional prices for these enhanced features. See HELP ALERT for more information.
***
--U.S. Patents Fulltext (File 654) has been redesigned with new search and display features. See HELP NEWS 654 for information.
***
--Connect Time joins DialUnits as pricing options on Dialog. See HELP CONNECT for information.
***
--CLAIMS/US Patents (Files 340,341, 942) have been enhanced with both application and grant publication level in a single record. See HELP NEWS 340 for information.
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--SourceOne patents are now delivered to your email inbox as PDF replacing TIFF delivery. See HELP SOURCE1 for more information.
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--Important news for public and academic libraries. See HELP LIBRARY for more information.
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--Important Notice to Freelance Authors--
See HELP FREELANCE for more information
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For information about the access to file 43 please see Help News43.
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NEW FILES RELEASED
***Dialog NewsRoom - Current 3-4 months (File 990)
***Dialog NewsRoom - 2002 Archive (File 993)
***Dialog NewsRoom - 2001 Archive (File 994)
***Dialog NewsRoom - 2000 Archive (File 995)
***TRADEMARKSCAN-Finland (File 679)